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Growth and Development Analysis of Unilateral Cleft Palate Patients at One, Five, and Ten Years

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Surgery

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Abstract & Key Words

Active and passive pre-surgical orthopedic (PSO) devices are a controversial part of cleft palate management. There is no consensus as to the effects of these PSO devices on long-term outcomes and there is limited research comparing different PSO devices. The first objective of this research was to perform a systematic review of the literature surrounding the long-term effects of PSO device use. The second was to analyze and compare 10-year nasolabial aesthetic outcomes between patients treated with an active PSO device, passive PSO device, or no device. The final objective was to analyze and compare 10-year dental occlusion and facial growth in patients who received treatment with an active versus a passive PSO device. All patient data was assessed at 1, 5, and 10 years. Nasolabial aesthetics were assessed using patient photographs, dental occlusion was assessed using dental molds, and facial growth was assessed through cephalometric analysis. Systematic review identified 41 articles pertaining to long-term effects of PSO device use. This systematic review didn't identify a consensus as to the effects of these devices but did identify that all 41 articles had methodologic flaws that limit the applicability of their results. Comparison of nasolabial aesthetics showed that patients treated with a PSO device have comparable aesthetics at the 10-year mark to patients treated with no device who have less severe alveolar gaps. Patients treated with active and passive devices have similar dental occlusion/arch development and facial growth up to 10 years.

Key words: cleft palate, cleft lip, pre-surgical device, pre-surgical orthopedics, latham device, nasoalveolar molding

Summary for Lay Audience

Patients born with cleft lip and palate are often treated with a pre-surgical device prior to the surgical repair of their cleft lip. The role of this device is to help decrease the size of the gap in their palate, which in turn brings the edges of the lip closer together to facilitate the surgical repair of the lip. These devices can be active or passive. Active devices drive the edges of the cleft closer together with a pin and screw device, whereas passive devices gradually mold the cleft with a plate. The use of these devices is still controversial. The devices have been shown to improve patient outcomes but have also been shown to limit facial growth in these patients. In addition, there is very little research that has compared outcomes in patients depending on which type of device they received. The objectives of this study were to (1) review the research that has been done on these devices to see their long-term effects on patient outcomes, and (2) look at the long-term effects of these devices on facial aesthetics, dental occlusion (how the teeth fit together), and facial growth in a group of patients that have received treatment with these devices.

The literature review identified that research into the long-term effects of these devices is lacking. The research that does exist is limited by studies of poor quality. In addition, very few studies actually compared active and passive devices to see if one type of device is superior. Aesthetic outcomes for patients that received active or passive device treatment was similar between groups; aesthetics were comparable to patients with less severe clefts that did not require a device. Facial growth and dental occlusion were assessed at 5 and 10 years in patients with an active or a passive device. Dental occlusion and facial growth were both similar for patients treated with an active or a passive device up to 10 years of age.

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Dedication

The preparation and completion of this thesis was made possible by the assistance of many individuals. Firstly, I would like to thank my supervisors Dr. Damir Matic, Dr. Timothy Foley, and Dr. Luc Dubois. Their support and expertise were essential for the completion of this work. Without their assistance I would not have succeeded in completing this project. Specifically, I would like to thank Dr. Matic for his assistance with the study design and mentorship throughout this entire project. Thank you for always feeding my passion for pediatric plastic surgery. I would like to thank Dr. Foley for all of his teaching on dental occlusion and cephalometric analysis. Finally, I would like to thank Dr. Dubois for his expertise in both the development of a systematic review and statistical analysis.

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List of Abbreviations

CL/P: Cleft lip/palate
CP: Cleft palate
LVP: Levator veli palatini
TVP: Tensor veli palatini
FNP: Frontonasal prominence
MXP: Maxillary prominence
LNP: Lateral nasal prominence
MNP: Mandibular prominence
PSO: Pre-surgical orthopedic
GPP: Gingivoperiosteoplasty
NAM: Nasoalveolar molding
MHB: Modified Huddart Bodenham
S: Sella turcica
N: Nasion
A: A-point
ANS: Anterior nasal spine
PNS: Posterior nasal spine
Ba: Basion
B: B-point
Pg: Pogonion
Me: Menton
N': Soft tissue nasion
A': Soft tissue A-point
Pg': Soft tissue pogonion
G': Soft tissue gnathion
Pn: Pronasale
Col: Columella
Sn: Subnasale
VPI: Velopharyngeal insufficiency

AG: Alveolar gap

Chapter 1: Introduction

This chapter introduces the current state of knowledge regarding cleft lip and cleft palate. The embryology, important surgical anatomy, and classification of the cleft lip and palate are reviewed. Current standards of care for the management of cleft lip and palate are reviewed including cleft lip repair, cleft palate repair, and pre-surgical orthopedic devices. Current methods of assessing outcomes in these patients including nasolabial aesthetic evaluation, dental arch/occlusion analysis, and cephalometric analysis are reviewed. The objective, purpose, rationale, and hypothesis of this work are also given.

1.1 EPIDEMIOLOGY OF CLEFT LIP AND PALATE

Cleft lip and palate are common pediatric craniofacial malformations (1). In Canada, the incidence of cleft lip and palate in newborns is 0.82:1000 and the incidence of isolated cleft palate is 0.58:1000 (2). Cleft lip and palate can also be associated with various syndromes including Stickler syndrome (25% of cases), velocardiofacial syndrome (15%), and van der Woude's syndrome (19%). Approximately 13.8% of cleft lip and palate, and 41.8% of isolated cleft palate, are associated with syndromes (3). A common triad of presentation in non-syndromic patients is the Pierre-Robin sequence which includes micrognathia/retrognathia, glossoptosis, and airway obstruction (3). The genetic association of non-syndromic cleft lip and palate is estimated at 20 to 50%, with environmental factors likely contributing to the remainder of cleft development (3). Environmental factors associated with the development of cleft lip/palate include maternal smoking, maternal corticosteroid use, folic acid deficiency, high altitude, and increased parental age (3).

1.2 EMBRYOLOGY OF CLEFT LIP AND PALATE

The pathogenesis behind the development of cleft lip and palate is complex and multifactorial. The entire pathophysiology behind the process is not known, and many studies in this domain are animal studies (4). The following is an overview of the current state of knowledge of the pathophysiology behind the development of cleft lip and palate.

Craniofacial tissues originate from neural crest cells and mesoderm. Neural crest cells migrate to the prominences of the face from the dorsal neural tube. During development in utero, the lip develops during the first 4 to 10 weeks of gestation and the palate develops between 4 to 12 weeks of gestation. The lip and palate are formed by the fusion of 7 facial prominences. Failure of the neural crest cells in these prominences to migrate to midline and fuse is what leads to cleft lip and palate deformities. Signaling molecules involved in the migration of neural crest cells to midline include Wnt, FOXE1, and IRF6 (3,4).

The face is formed by 7 facial prominences (Figure 1): the frontonasal prominence, bilateral maxillary prominences, lateral nasal prominences, and the bilateral mandibular prominences. The frontonasal prominence gives rise to the forehead, central nose, philtrum, middle of the upper lip, and the primary palate. Interruption in the growth of the frontonasal prominence leads to bilateral cleft lip. The maxillary prominences give rise to the upper jaw, sides of the face, sides of the upper lip, and the secondary palate. Disruption of maxillary prominence growth can lead to clefts of the secondary palate and the lip. The lateral nasal prominences give rise to the nasal alae. Failure of fusion between the lateral nasal prominences and the frontonasal/maxillary processes can lead to clefts of the side of the nose. The mandibular prominences give rise to the lower jaw and lower lip. Disruption in growth of the mandibular prominences can result in mandibular clefts, although this is quite rare. Failure of fusion between the frontonasal and maxillary processes results in clefts of the primary palate (3,4).

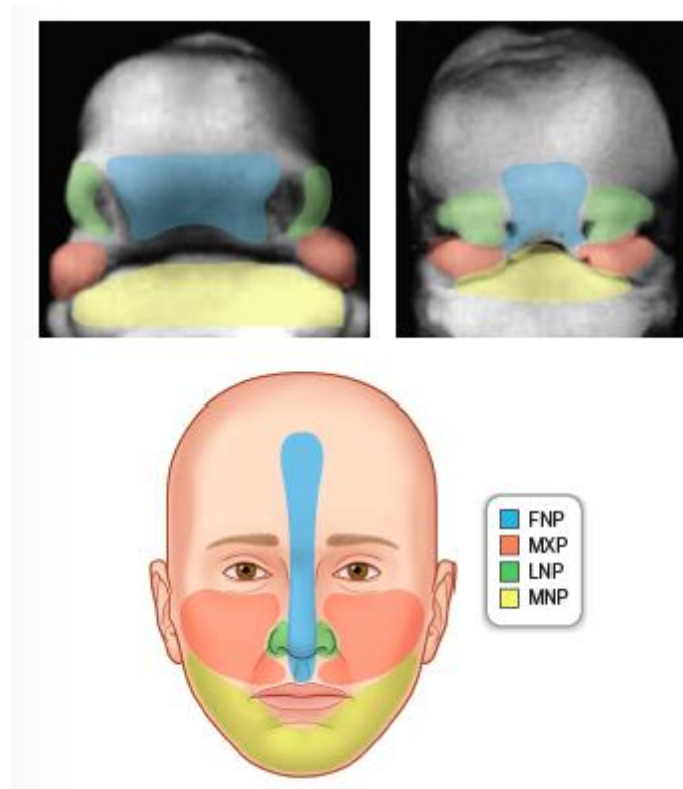


Figure 1: Reproduced from Neligan et al. with permission from Elsevier publishing (4). Embryonic facial prominences and their corresponding adult facial structures. FNP= frontonasal prominence; MXP= maxillary prominence; LNP= lateral nasal prominence; MNP= mandibular prominence.

1.3 CLEFT CLASSIFICATION

There are several important definitions used when describing cleft lip and palate. Clefts can occur in the primary or the secondary palate. The primary palate extends from the base of the nasal processes to the incisive foramen of the alveolus. The secondary palate extends from the incisive foramen to the uvula. Clefts can be classified as unilateral or bilateral. Unilateral clefts are isolated to one side of the primary/secondary palate (either left or right) and bilateral clefts involve both sides. Clefts are also described as complete or incomplete. A complete cleft of the primary or secondary palate involves the entire unit of the palatal structure, whereas an incomplete cleft palate does not (4). See Figure 2 for examples of cleft classification.

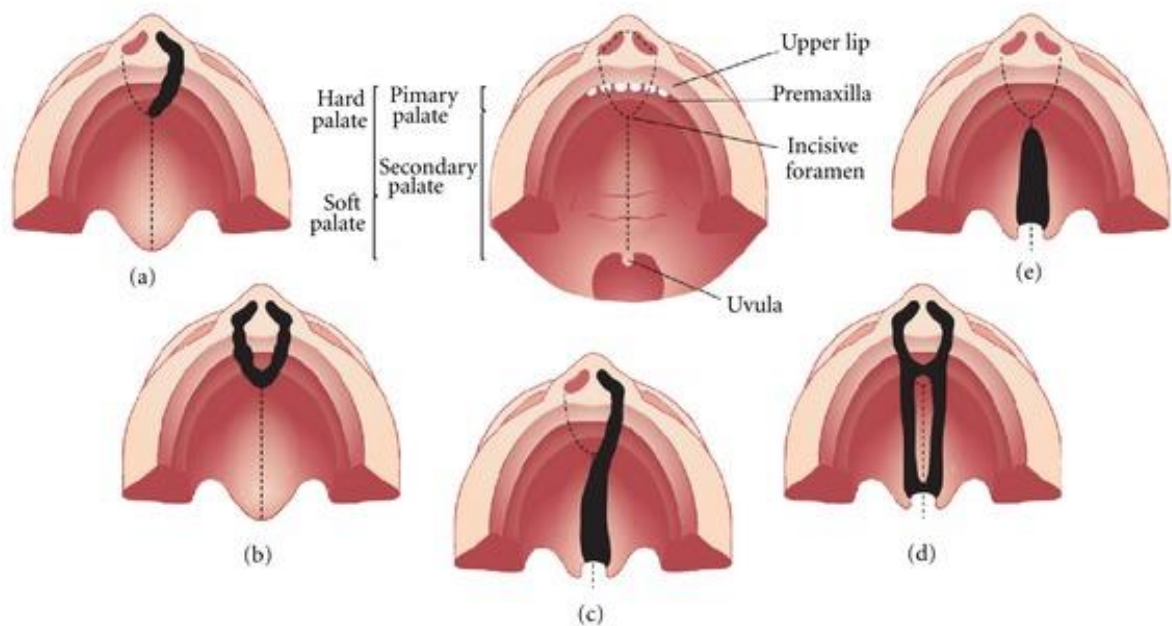


Figure 2: Copyright Brito et al. (5), open access figure. Normal palate anatomy (upper middle image). (A) Unilateral complete cleft of primary palate, (B) Bilateral complete cleft of primary palate, (C) Unilateral complete cleft of primary and secondary palate, (D) Bilateral complete cleft of primary and secondary palate, (E) Complete cleft of secondary palate.

1.4 SURGICAL ANATOMY OF THE CLEFT LIP

The anatomy of the lip is important for understanding the principles behind surgical repair and assessing post-operative outcomes. The following is a brief overview of lip anatomy and changes in the anatomy associated with cleft lip.

The lip itself is composed of several surface landmarks: philtral columns, philtral dimple, Cupid's bow, vermillion border, and the vermillo-mucosal junction (Figure 3). The philtral columns are created by the insertion of the orbicularis oris muscle fibers, and the philtral dimple is the concavity created by the paucity of muscle fibers between the two columns. The Cupid's bow is the curve of the upper lip between the two philtral columns. The vermillion is the border between the red lip and the adjacent normal skin. The vermillo-mucosal junction is the border between the dry (keratinized) and the wet (non-keratinized) portions of the lip. Nose anatomy is also important when discussing clefts of the primary palate. Important structures of nasal anatomy include the alar base, the nasal tip, the nostrils, and the columella (Figure 3).

There are 2 principle muscles that are relevant to the surgical repair of the cleft lip, the orbicularis oris and the levator labii superioris. The orbicularis oris muscle functions to move the lips for speech, facial expression, and eating. The levator labii superioris functions to elevate the upper lip. The lips receive their blood supply from bilateral superior labial arteries, their sensory innervation from the V2 of the trigeminal nerve, and motor innervation from the facial nerve (3).

In patients with a cleft of the primary palate involving the lip, the orbicularis oris muscle inserts at the alar wing (at the edge of the cleft) instead of its usual insertion at the mucous membrane of the lip. There is also hypoplasia of the pars marginalis (a component of the orbicularis oris). A cleft of the primary palate involving the lip also causes shortening of the philtrum, diminished vermillion width on the non-cleft side, and increased vermillion width on the cleft side (3). A complete cleft of the

primary palate can cause multiple nasal deformities including nasal tip deviation, septal deviation (to the non-cleft side), widened and inferiorly positioned alar base (cleft side), collapsed lateral cartilage (cleft side), columellar shortening (cleft side), and inferior turbinate hypertrophy (cleft side) (3).



Figure 3: Original photograph of important nasolabial landmarks. (1) Philtral column, (2) Philtral dimple, (3) Cupid's bow, (4) Vermillion, (5) Vermillo-mucosal junction, (6) Alar Base, (7) Columella, (8) Nostril, and (9) Nasal tip.

1.5 SURGICAL REPAIR OF THE CLEFT LIP

The objective of surgical repair of the cleft lip is anatomic re-creation of normal lip elements (Figure 3) and maintenance of the vertical height of the lip (6). When performing cleft lip repair the skin, muscle, and mucosal layers must be re-aligned (6). The most common repair techniques are the rotation advancement flap by Millard, triangular flap technique by Tennison, wave line closure by Pfeifer, and functional repair by Delaire. The techniques vary in their incision lines, but ultimately aim to restore anatomic alignment of the lip (7,8).

In patients with a complete primary cleft palate, the alveolar gap makes lip repair difficult. Pre-surgical orthopedics (PSO) are frequently used in patients with large alveolar gaps prior to lip repair. The purpose of PSOs is to decrease the gap size, bring the lip elements closer together, re-establish the palatal arch, and aid with intra-oral feeding (9–11). Pre-surgical orthopedics include lip taping, lip adhesion, and PSO devices (11,12). On average, the surgical management of cleft lip is usually undertaken when the child is close to 3 months of age and PSOs are undertaken soon after birth and used until the time of lip repair (6).

At the time of lip repair, a gingivoperiosteoplasty (GPP) can also be performed to close the alveolar gap. The purpose of a GPP is to close the alveolar gap, reduce the necessity for bone grafting, and recreate an anatomic palatal arch (13,14).

1.6 SURGICAL ANATOMY OF THE CLEFT PALATE

The anatomy of the palate is important for understanding how cleft palate is managed and for assessing post-operative outcomes. The following is a brief overview of palate anatomy and changes in the anatomy associated with cleft palate.

The palate is composed of the hard and the soft palate (Figure 2). The hard palate is the boney structure that functions as a rigid floor for the nasal cavity. The hard palate is composed of the premaxillary portion, the palatine processes of the maxilla, and the palatine processes of the palatine bone. The hard palate receives its blood supply from the greater palatine, nasopalatine, anterior superior alveolar, and posterior superior alveolar arteries. The hard palate receives its innervation from the greater palatine and nasopalatine nerves. The soft palate is the fibromuscular structure posterior to the hard palate that moves to open and close the Eustachian canals. The muscles that form the soft palate include the levator veli palatini, tensor veli palatini (TVP), palatopharyngeus, palatoglossus, the musculus uvulae, superior pharyngeal constrictor, salpingopharyngeus, and the stylopharyngeus. Blood supply to the soft palate originates from the ascending pharyngeal and ascending palatine arteries. Innervation is supplied by the cranial nerve 5 (TVP only) and pharyngeal plexus (remaining muscles) (3).

The palate can further be divided into the primary palate and secondary palate. The primary palate lies anterior to the incisive foramen and includes the lip, nostril sill, alveolus, and the portion of the hard palate that is anterior to the incisive foramen. The secondary palate lies posterior to the primary palate and includes the hard palate posterior to the incisive foramen and the soft palate (3).

Changes to palate anatomy vary depending on the extent of the cleft. Typically, muscle fibers of the involved muscles are hypoplastic and more connective tissue lies within the muscular bed (3).

1.7 SURGICAL REPAIR OF CLEFT PALATE

The objective of surgical repair of the cleft palate is to allow for good speech development, velopharyngeal function, and midface development. Three layers must be addressed in palate repair: the nasal layer, the muscle layer, and the oral mucosa layer. Techniques for palate repair include the von Langenbeck palatoplasty, Veau-Wardill-Kilner palatoplasty, Furlow double opposing Z-platoplasty, vomer flaps, and the intra-velar veloplasty (7,8).

Repair of the palate can either be done in 1 stage or 2 stages; 2-stage repair involves fixing the hard and soft palate at 2 separate times. Two stage repair is beneficial for midface growth, but does have a detrimental effect on speech development in addition to the need for an additional operative procedure and anesthesia (7). It is still unclear from the literature which technique/method results in the best speech outcomes with the least effect on growth (15–20).

1.8 TIMING OF SURGERY

Timing of surgery for cleft lip and palate is crucial for proper growth and speech development and is still highly debated among cleft palate surgeons. It has been shown in the literature that patients with untreated cleft lip and palate have normal growth of the nasomaxillary complex (21,22), whereas patients who have had lip and palate repairs have diminished growth (23). Ultimately, this indicates that surgical management may cause limitations in growth. This presents cleft surgeons with the challenge of balancing the timing of cleft palate repair for appropriate speech development, while limiting the negative impact on growth.

Advocates for early surgical management believe that surgical closure of the palate allows for improved speech development, while advocates of late palate closure believe that the closure itself causes a growth deficit (24–26). Previous research from the Oxford Cleft Palate Study Team shows greater speech deficiencies (articulation, nasal resonance, intelligibility and substitution pattern) in patients with delayed hard palate closure (4 years) compared to those with early palate closure (1 year) (27). No difference in maxillofacial growth was found between the groups. Conversely, Bardach et al. found improved facial growth in patients with delayed hard palate closure (up to 12-15 years), but higher incidence of velopharyngeal insufficiency (25). Rohrich et al. studied outcomes in patients with early versus delayed closure and found that delayed closure resulted in significant speech impairments with little difference in overall maxillary growth (27). Shaffer et al. also found higher rates of language delay and need for speech therapy in patients with delayed palate repair (over 13 months) (28). Evidence from the Scandcleft studies have demonstrated no significant difference in dental arch or maxillary development in patients who had palatal surgery at 12 versus 36 months (29,30).

Overall, the timing for palate surgery is still highly debated. The trend with cleft palate surgeons in North America is to perform a single stage cleft palate surgery at 9 to 12 months of age for improved patient speech outcomes and reduced risk of maxillary growth disturbance (31–34).

1.9 MANAGEMENT OF CLEFT LIP AND PALATE AT OUR INSTITUTION

At our institution the management of patients with cleft lip and palate is a multi-staged, multi-disciplinary approach involving plastic surgery, otolaryngology, speech and language therapy, social work, and dentistry (34). The primary goal of cleft palate surgery is to achieve satisfactory functional (e.g. eating, speech) and aesthetic results (1).

At our institution, cleft lip repair is usually performed at 3 months of age and cleft palate repair is performed at 12 months. All patients with a cleft lip receive a modified Mohler lip repair. Patients with a cleft of the secondary palate receive a Furlow palatoplasty, hybrid palatoplasty, or von Langenbeck palatoplasty depending on whether the cleft is complete or incomplete. Pre-surgical orthopedic devices are often used to narrow the alveolar gap and facilitate intra-oral feeding prior to cleft lip repair. At our institution, the decision to use a PSO device is made at the first clinic visit which is usually 1 to 2 weeks post-birth. Families with a patient that has an alveolar gap greater than 4mm are offered pre-surgical management with a PSO device. If the patient is to receive a PSO device, they are sent to an orthodontic specialist where a plaster cast of their cleft is made. This cast is used to design either an active or a passive molding device. Passive molding devices can be inserted in the office, but active PSO devices require insertion in the operating room under general anesthesia. Active devices require parents to turn a screw on the device daily to re-approximate the edges of the cleft. For a passive device, the patient and caregiver are expected to come for regular follow-ups visits to gradually mold the device. The decision of which PSO device to use is made based on the severity of the alveolar gap, the caregiver's capacity to handle care of the device at home, and caregiver preference. Figure 4 gives a visual representation of the management protocol that a patient with cleft lip and palate receives at our institution.

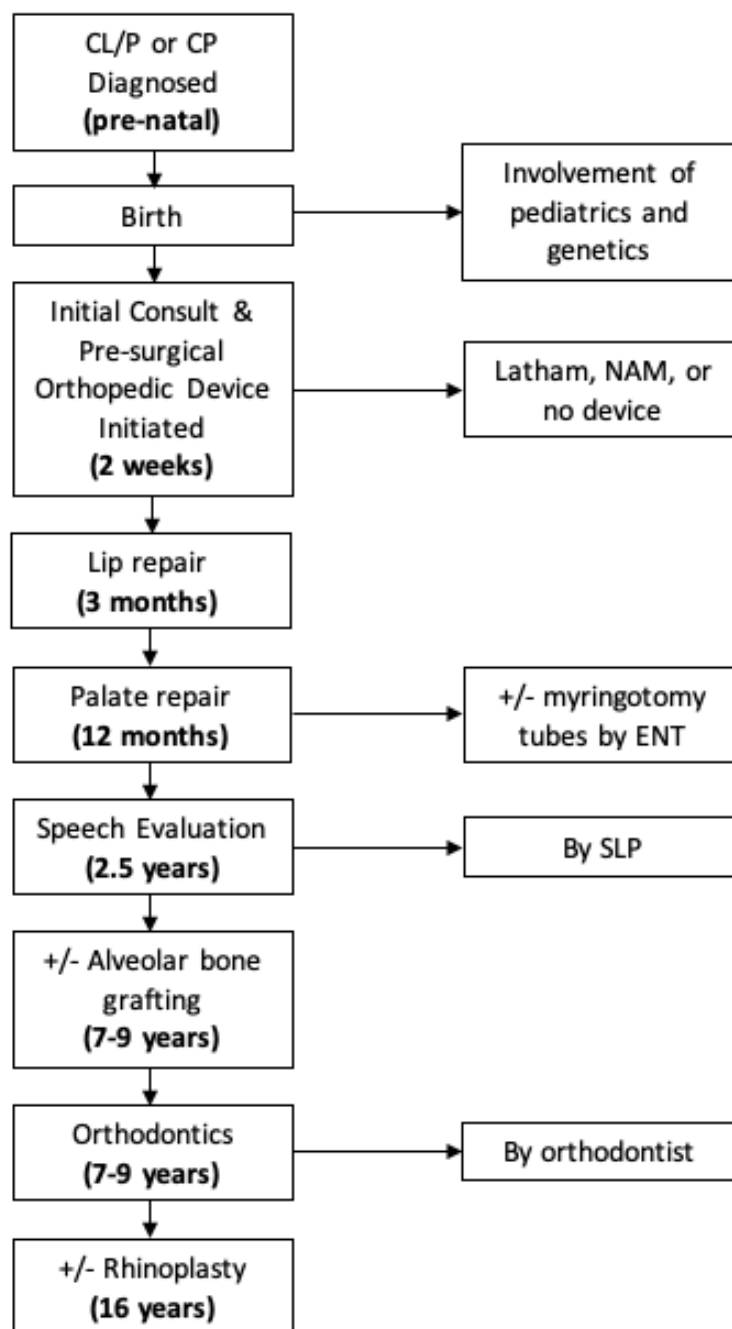


Figure 4: Overview of management process for CL/P and CP patients at our institution. ENT= otolaryngology, SLP= speech language pathology.

1.10 PRE-SURGICAL ORTHOPEDIC DEVICES

1.10.1 Active Devices

Active PSO devices are designed to drive the edges of the alveolar gap closer together using pins or screws (35). One of the most commonly used active devices is the Latham appliance. It was first introduced by Latham and Millard in 1990 (36). The Latham appliance (Figure 5) is a pin-retained intra-oral device that utilizes a mechanical screw that is turned daily by the parents to approximate the edges of the alveolar gap by approximately 0.5mm per day (37–39).

Active devices were initially designed to be used in conjunction with GPP to narrow the alveolar gap prior to lip repair to facilitate the repair and prevent dehiscence (40,41). Multiple studies have shown that active devices and GPP improved aesthetic outcomes, allowed for adequate maxillary growth, and decreased the number of nasoalveolar fistulas (37,41,42). Unfortunately, active devices in conjunction with GPP have also been identified to cause decreased maxillary protrusion and height throughout development, reduce successfulness of secondary bone grafting, and have no effect on the number of patients that require secondary bone grafting (43,44). Following these more recent studies, the use of GPP in patients has decreased significantly.

The effect of the active device alone is still debated. Lin et al. have found that the active device is associated with an increased incidence of ectopic permanent maxillary first molars compared to patients without a device (45). Chan et al. have shown that compared to patients treated with no device, there is no difference in long-term (10-year) dental occlusion or growth in children treated with an active device (46). Kornbluth et al. have also shown that active devices are associated with improved nasolabial aesthetic outcomes, but cause a midface growth disturbance (35). Overall, there is still no conclusion about the effects of the active

device and high level evidence is lacking (35). Further research must be done to establish the effect of the active device without GPP on growth outcomes in patients with cleft lip and palate.

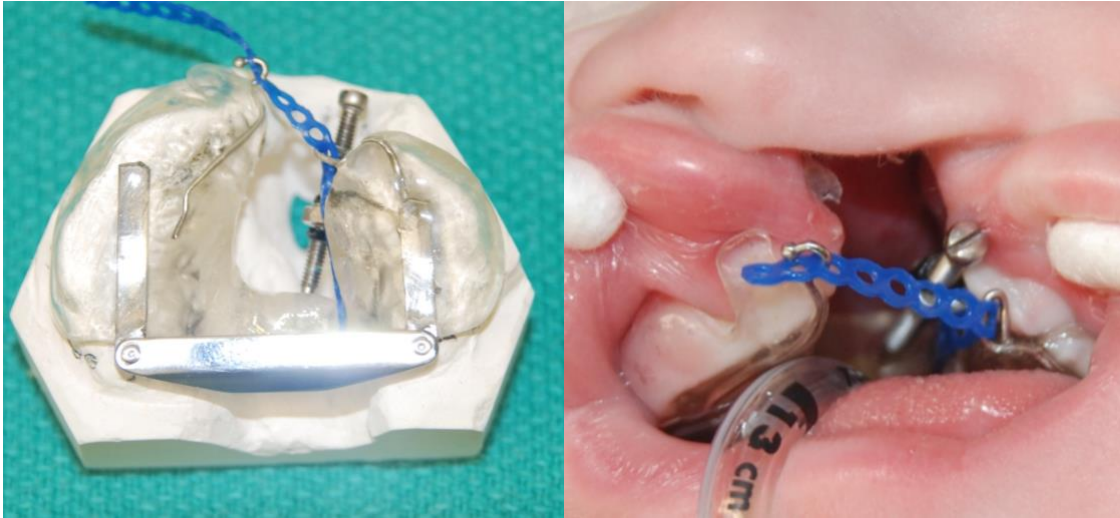


Figure 5: The Latham device is pictured above on a patient mold (left) and in-situ (right).

1.10.2 Passive Devices

Passive PSO devices have the same overall objective as active PSO devices, but do not actively drive together the edges of the alveolar gap. Instead, passive devices are intra-oral plates that are custom fit to patients. These devices are modified weekly to help bring the oronasal structures into a more anatomic position. Ideally, passive molding is started in the first week of life and used in patients with a cleft of 3 to 8mm (47). Passive PSO devices work because of the plasticity of neonate cartilaginous and bony structures shortly after birth (47,48). An example of a passive PSO device is the nasoalveolar molding (NAM) device (Figure 6). NAM was first described in 1993 by Barry Grayson and works by molding the alveolar segments and nose through a custom-fit intra-oral appliance with nasal stents.

Multiple studies have shown that when compared to the contralateral non-clefted side, passive devices appear to improve several aesthetic factors including columella length, columella deviation, nostril width, and nasal height (48–50). Passive devices have also been shown to improve nasolabial aesthetic outcomes when compared to patients treated without a PSO device (51,52). In regards to the effect of these devices on growth, it has been shown that they decrease the size of the alveolar gap in the short term (less than 2 years of age) (53,54). Previous studies have compared patients who received a passive device to those who did not, and passive molding has been shown to improve dental arch symmetry and maxillary growth until 6 years of age (54).

Contrasting evidence has also been published on passive molding. Prah et al. as part of the Dutchcleft study group showed that passive PSO devices do not improve contact between the alveolar segments of the cleft or prevent long-term (6-year) alveolar collapse (55,56). Similar results have been found by other groups (57,58). Studies have also proposed that passive molding provides no improvement in nasolabial aesthetics compared to patients who received no

device (59). With respect to the effect on dental development and facial growth, several studies have shown no long-term effects of passive molding on maxillary growth and dental arch relationships when compared to patients treated with no device (46,55,56),

Overall, the benefits of passive PSO devices are still debated. One of the most strongly supported benefits is that passive devices can help improve nasal aesthetics and narrow the cleft (48,49). There is limited research that actually examines the long-term benefits of passive molding (54,60).



Figure 6: Original photograph. A custom-made NAM device is pictured above.

1.10.3 Comparing Active and Passive Devices

In the field of cleft palate research there are very few studies comparing active versus passive molding devices. The trend in cleft palate management is to either use active molding or passive molding, and there is very limited data that actually compares the two methods of molding. Kornbluth et al. have compared patient outcomes that were treated with active or passive devices compared to those treated without a device (35). Unfortunately, this study did not report statistics for the comparison between the active and passive device groups specifically, although they appeared to have similar results between the two groups for nasolabial aesthetics, facial growth, and dental occlusion. A major limitation in this study was that patients in the different device groups were treated by different surgeons using different management protocols. It is difficult to compare outcomes in patients treated with active versus passive devices when these confounding variables could influence results. A comparison of active and passive molding techniques where confounding variables are eliminated would be beneficial for determining if certain techniques are superior for patient outcomes including midface growth, dental occlusion, and nasolabial aesthetics (35).

1.11 METHODS OF ASSESSING POST-OPERATIVE AESTHETIC OUTCOMES

1.11.1 Nasolabial Aesthetics

Patients with cleft lip and palate undergo multiple surgical interventions in order to ensure adequate functional and anatomic correction of the cleft deformity (61). Despite these corrections, patients have been found to have persistent anatomic deformities including abnormal nasal shape, scarring of the upper lip, and uneven vermillion border (62,63). While certain studies have reported no psychosocial concerns for patients with cleft lip and palate compared to patients without, several systematic reviews have shown that patients with cleft lip/palate are at higher risk for dissatisfaction with facial appearance, behavioural problems, and impairment in social functioning (64,65). Therefore, it is important to use an objective assessment tool for evaluating nasolabial aesthetic outcomes to ensure satisfactory aesthetic results.

Aesthetic scales are frequently used in plastic surgery to assess post-operative outcomes and the same tools are used for assessing outcomes in patients with cleft lip/palate. Scales used to assess nasolabial aesthetics can be divided into quantitative and qualitative scales. Quantitative scales use specific anthropometric measurements to evaluate different soft tissue landmarks on patient photographs for overall symmetry (66,67). Qualitative scales are used to evaluate aesthetics on patient photographs and include ordinal scales, visual analog scales, and ranking scales (62). Previous research shows that ranking scales have the greatest intra-rater reliability, followed by visual analog scales and ordinal scales (63). Historically, 2-dimensional (2-D) photographs have been used to assess post-operative outcomes, but studies have begun using 3-dimensional (3-D) images as well. When comparing 2-D and 3-D images, 3-D images have greater intra-rater reliability but scoring of patients evaluated with the two modalities is not different (68).

The focus of nasolabial aesthetic assessment in patients with cleft lip and palate is often on nasal form, nasal symmetry, vermillion border form, and lip symmetry. These aspects of the nose and lip are disrupted in cleft lip/palate and repair is meant to bring the nose and lip back into an anatomic position (61,69). Important components of nasolabial aesthetic outcomes include the scar, alar base symmetry, columellar deviation, nasal tip recurvatum, nostril symmetry, Cupid's Bow symmetry, the vermillo-cutaneous junction, and the vermillo-mucosal junction (Figure 7) (61,69).

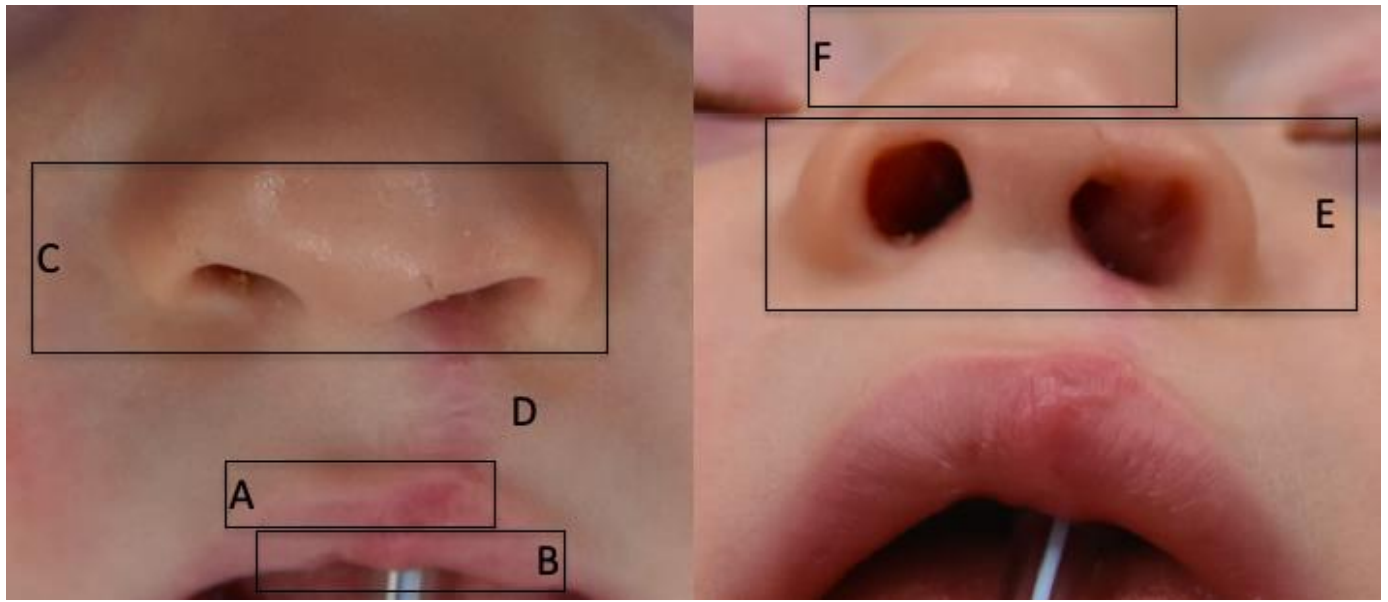


Figure 7: Original photographs. Important landmarks to assess nasolabial aesthetics include (A) symmetry of Cupid's Bow and the vermillo-cutaneous junction, (B) symmetry of the vermillo-mucosal junction, (C) alar base symmetry, (D) scar quality and position, (E) nostril symmetry, and (F) nasal tip symmetry.

1.12 METHODS OF ASSESSING POST-OPERATIVE GROWTH OUTCOMES

1.12.1 Angle Classification

Dental occlusion is defined as the way in which the maxillary and mandibular teeth fit together. Classically, occlusion is described using the Angle classification. The Angle classification is the gold standard for describing occlusion and was initially developed in the 1890's to describe dental occlusion based on the position of the mesiobuccal cusp of the maxillary first molar to the buccal groove of the mandibular first molar (70). The Angle classification system is as follows (Figure 8): (1) Normal occlusion, (2) Class I having normal molar relationship despite tooth rotation or crowding, (3) Class II having lower molars distal to upper molars, and (4) Class III having lower molars mesial to upper molars (71).

The Angle classification system is widely used for classifying occlusion but has been criticized for being a 2-D classification of a 3-D problem. The Angle classification is useful for characterizing sagittal occlusion, but other scoring systems have been described for assessing occlusion in a 3-D way.



Figure 8: Original images. Angle classification system of occlusion.

1.12.1.1.1 GOSLON Yardstick

Several different methods for scoring dental arch relationships have been used in the CL/P population. The GOSLON Yardstick is the gold standard for measuring skeletal and dental relationships in patients with CL/P and was first developed in 1987 (35,72). The GOSLON Yardstick classification rates the occlusion into 1 of 5 categories using the anteroposterior, vertical, and sagittal dimensions of 3-D casts of patients' mouths. This classification system provides a general prediction about future requirements for surgery (73). The GOSLON Yardstick is based on the distance between the incisal edge of the maxillary incisors and the labial surfaces of the mandibular incisors, termed "overjet". The five grades are as follow:

Group 1	Positive overjet	Minimal or no treatment required
Group 2	Positive overjet	Minimal treatment required
Group 3	Edge to edge bite	Orthodontic treatment required, but good outcome anticipated
Group 4	Negative overjet (1-3mm)	Orthodontic treatment required with possible future orthognathic surgery
Group 5	Negative overjet (>3mm)	Definite orthognathic surgery required

The GOSLON yardstick is a useful tool for analyzing occlusion and predicting the need for future orthognathic intervention (74). See Figure 9 for photographs of patient molds with different grades of occlusion.

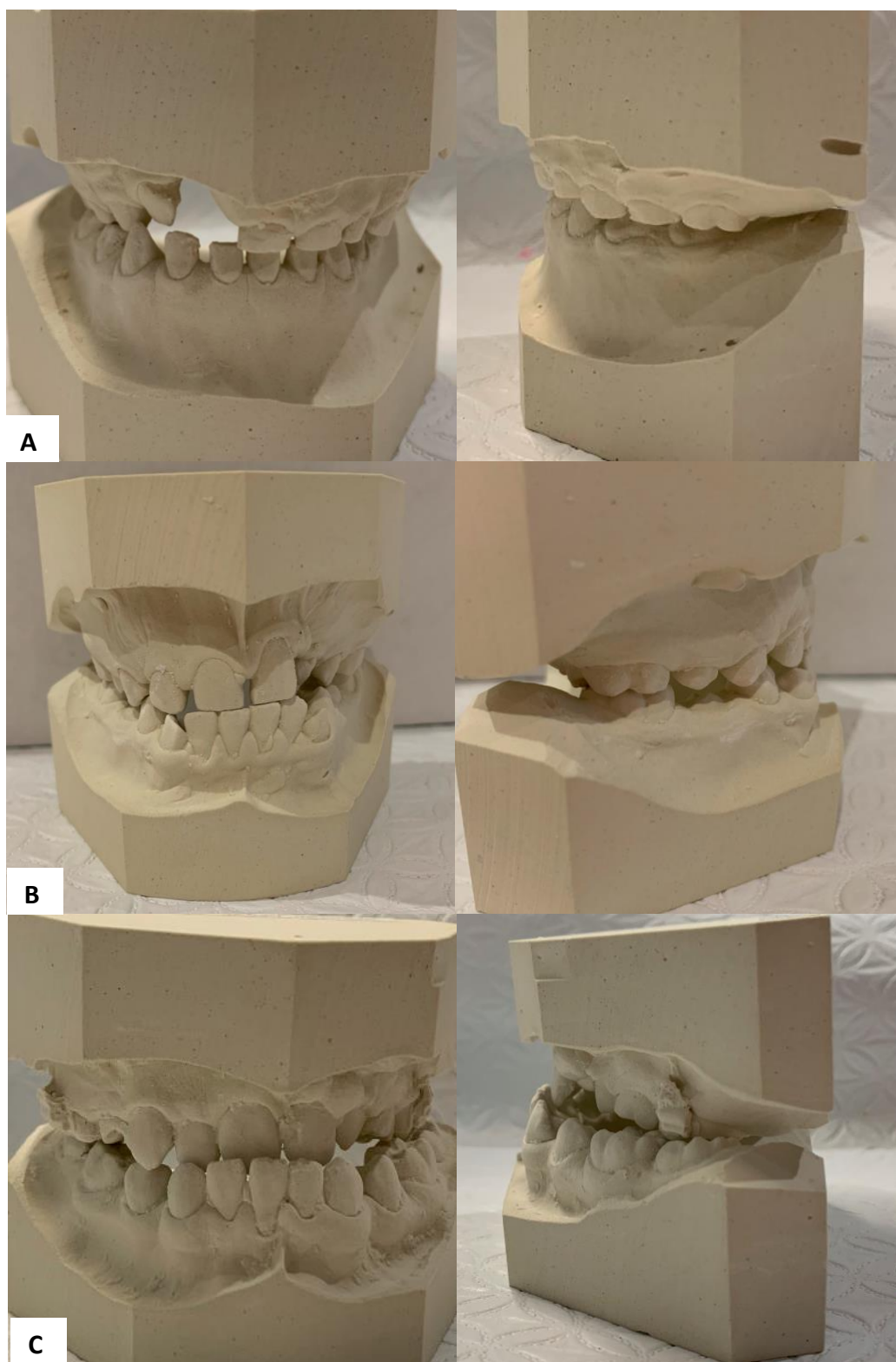


Figure 9: Original photographs. Patient molds representing: (A) Positive overjet, GOSLON Yardstick Grade 1/2; (B) No overjet, GOSLON Yardstick Grade 3; (C) Negative overjet, GOSLON Yardstick Grade 4/5.

1.12.2 Modified Huddart/Bodenham Classification

The Modified Huddart/Bodenham (MHB) classification is another classification system of dental occlusion that was initially developed in 1997 for primary dentition and modified in 2003 to apply to mixed/permanent dentition (75). The MHB system classifies the position of each maxillary tooth in relation to its mandibular tooth partner. Each relationship is given a score from -3 to +1 and the mean score for each relationship is calculated (Figure 10); a more negative score indicates worse dental relationships. In primary dentition, the two central incisors, bilateral canines and bilateral molars are measured to total 8 categories of evaluation. In primary dentition the total MHB score can range from -24 to +8. In mixed/permanent dentition the two central incisors, bilateral canines, bilateral pre-molars, and bilateral first permanent molars are measured to total 10 categories of evaluation. In mixed/permanent dentition the total MHB score can range from -30 to +10 (75).

In regard to whether the GOSLON yardstick or the MHB classification is superior for classifying occlusion, this is still highly debated. In the literature, both have been favored for different reasons. The MHB system is less subjective than the GOSLON Yardstick and appears to be more versatile for primary versus permanent dentition (30,76). The GOSLON Yardstick is more user-friendly and has been used for much longer than the MHB (76). Ultimately, controversy still remains about which classification system is best. Comparative studies have shown that MHB has been found to be superior for 5-year (primary) dentition, but GOSLON Yardstick is preferred for 10-year (permanent) models (72,76).

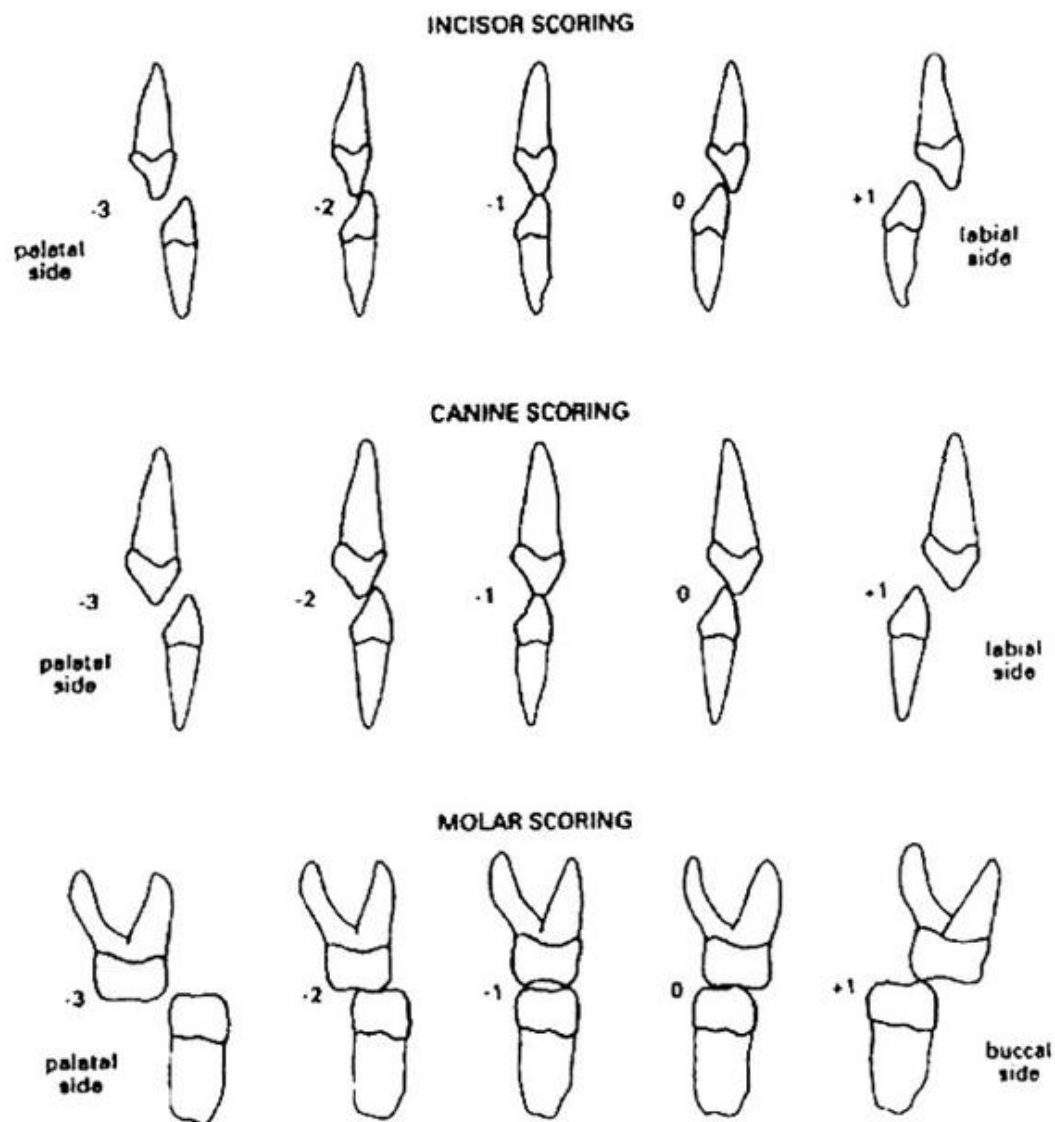


Figure 10: Reproduced with permission from Sage Publishing. Modified Huddart Bodenham classification of molars, canines, and incisors.

1.12.3 Dental/Occlusal Changes in Cleft Lip & Palate

Cleft lip and palate can produce a variety of dental problems including missing/additional teeth and abnormal shape and position of both deciduous and permanent teeth. Most commonly, teeth in the area of the cleft are affected. The most common orthodontic problem in patients with CL/P is maxillary asymmetry causing crossbite formation (7). The overall effect of cleft size on dental occlusion is still debated. Some authors have found that there is no relationship between the size of the cleft and occlusion (77,78). Conversely, several studies have shown that initial cleft size negatively affects maxillary inclination, which in turn affects occlusion (74,79). The effect of cleft size on dental arch and occlusal relationships is more likely to be multifactorial, with type and timing of palate repair also affecting the outcome (74).

1.12.4 Palatal Measurements

The width of the anterior and posterior palate represents the overall width of the palate and is important for understanding the space that the dental arch has for the teeth. The inter-canine width (ICW) and sum of the incisors (SI) represent the width of the anterior dental arch, and the inter-palatal molar width (IPMW) represents the width of the posterior dental arch (80). Inter-canine width is the distance between the maxillary canine grooves and IPMW is the distance between the retromolar points of the maxillary permanent first molars or deciduous second molars. The sum of the incisors is the maximum mesiodistal size of each of the four incisors (81). Reduction in maxillary dental arch width is a common concern with cleft palate and measuring arch width can help monitor growth and development of the dental arch. See Figure 11 for important dental arch measurements.

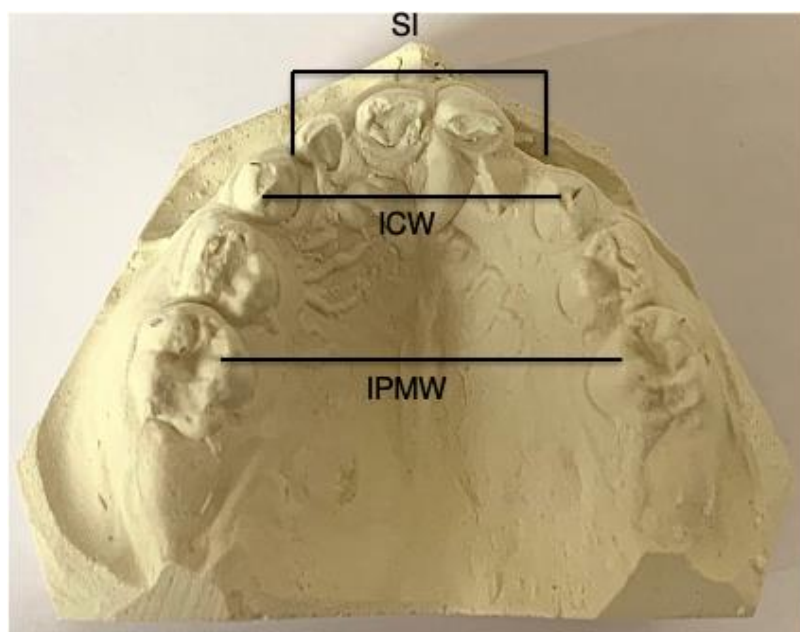


Figure 11: SI= sum of incisors, ICW= inter-canine width, IPMW= inter-palatal molar width

1.12.5 Cephalometric Analysis

Cephalometric measurements represent the gold standard for measuring facial growth and development (35). Cephalometric landmarks are plotted on lateral facial radiographs and used to analyse hard tissue points of interest that affect facial features. Historically, radiographs have been traced by hand to plot landmarks. More recently, programs such as Dolphin Imaging™ have been designed to plot landmarks and calculate measurements electronically (82).

There are two main functions of cephalometric analysis: (1) to compare facial morphology against a matched norm and (2) to assess facial growth in a patient (82). Cephalometric measurements can help monitor stability of the facial skeleton and determine whether surgical intervention is required to help correct deformity.

Traditionally, hard tissue markers have been used for cephalometric analysis. Boney landmarks do not predict soft tissue changes, so soft tissue traits must also be taken into consideration when analyzing facial morphology (83). Cephalometric analysis has now been modified to include soft tissue points of interest to help better analyze facial growth outcomes. Important boney cephalometric landmarks include sella turcica (S), nasion (N), A-point (A), posterior nasal spine (PNS), anterior nasal spine (ANS), basion (Ba), B-point (B), pogonion (Pg), and menton (Me) (Figure 12) (44,82–84). Important soft tissue landmarks include glabella (G'), pronasale (Pn'), soft tissue pogonion (Pg'), columella (Col), subnasale (Sn), upper lip (UL), soft tissue A-point (A'), soft tissue nasion (N'), and soft tissue B-point (B') (Figure 13) (44,82–84).

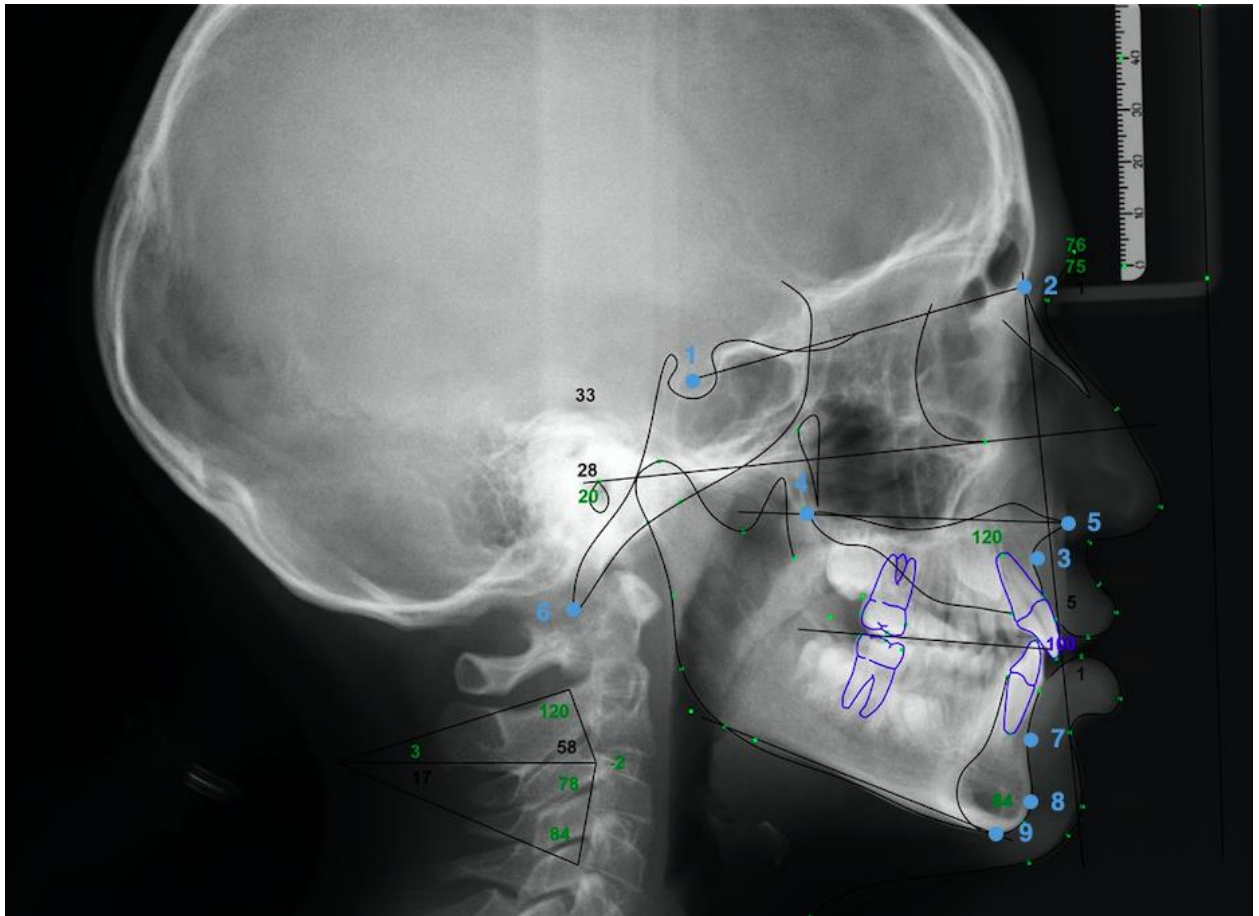


Figure 12: Original photograph. Cephalometric tracing of lateral patient x-ray. Important bone landmarks identified (in blue). (1) Sella Turcica, (2) Nasio, (3) A-point, (4, 5) Posterior and Anterior Nasal Spine, (6) Basion, (7) B-point, (8) Pogonion, (9) Menton.

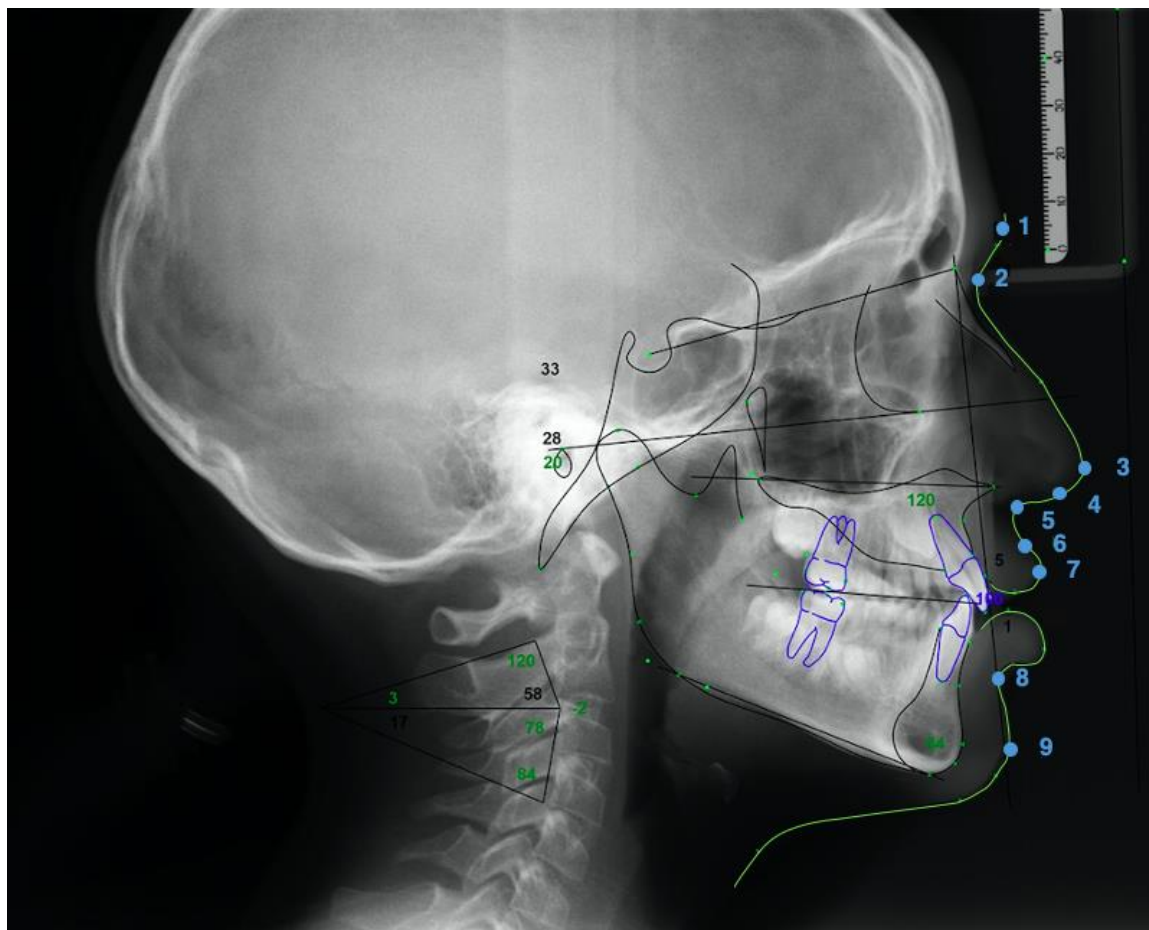


Figure 13: Original photograph. Cephalometric tracing of lateral patient x-ray. Important soft tissue landmarks identified (in blue). (1) Glabella, (2) Nasion, (3) Pronasale, (4) Columella, (5) Subnasale, (6) A-point, (7) Upper lip, (8) B-point, (9) Pogonion.

1.12.6 Brief Overview of Important Facial Relationships

There are five functional components of a cephalogram: cranial base/cranium, skeletal maxilla, skeletal mandible, maxillary dentition, and mandibular dentition. There are two ways of standardizing cephalograms with a horizontal reference plane: the Frankfort plane or the natural head position. The Frankfort plane creates a horizontal reference plane between the external auditory meatus to the anterior inferior orbital rim. The natural head position parallels the patient's visual axis by having the patient look at an object at the distant horizon (85).

Cephalometric analysis is important for analysis of growth, but these boney relationships can also help describe occlusion and predict facial attractiveness in patients. In addition, there exist some soft tissue relationships that are also predictive of facial attractiveness (85). These relationships can be quantified using cephalometric analysis. Cephalometric landmarks act as the foundation to create different cephalometric measurements that reflect important areas of facial growth and development. See Table 1 for a list of common cephalometric measurements and their importance for analyzing growth.

	Landmarks	Definition
Maxilla	SNA	Position of maxilla relative to anterior cranial base
	N-A	Horizontal distance between nasion and A-point
	PNS-ANS	Maxillary length
	Ba-A	Depth of midface
	Ba-ANS	Length of maxilla
	Ba-N-ANS	Maxillary position at ANS
	Ba-N-A	Maxillary position at A-point
Mandible	SNB	Position of mandible relative to anterior cranial base
	N-B	Horizontal distance between nasion and B-point
	N-Pg	Horizontal distance between nasion and pogonion
	Ba-N-Pg	Mandibular position at pogonion
	Ba-N-B	Mandibular position at B-point
Dento-alveolar	ANB	Relative position of maxilla to mandible
	ANS-N-A	Alveolus to basal bone measurement
	ANS-N-Pg	Basal bone difference
Vertical Face	N-ANS	Upper facial height
	ANS-Me	Lower facial height
	N-ANS/ANS-Me	Upper to lower face ratio
	N-ANS/N-Me	Midface percentage of total facial height
Soft Tissue	N'-A'-Pg'	Soft tissue convexity
	Gn'-Sn-Pg'	Facial contour angle
	Col-Sn-UL	Nasolabial angle

Table 1: Important cephalometric measurements and the growth parameters that they represent (56).

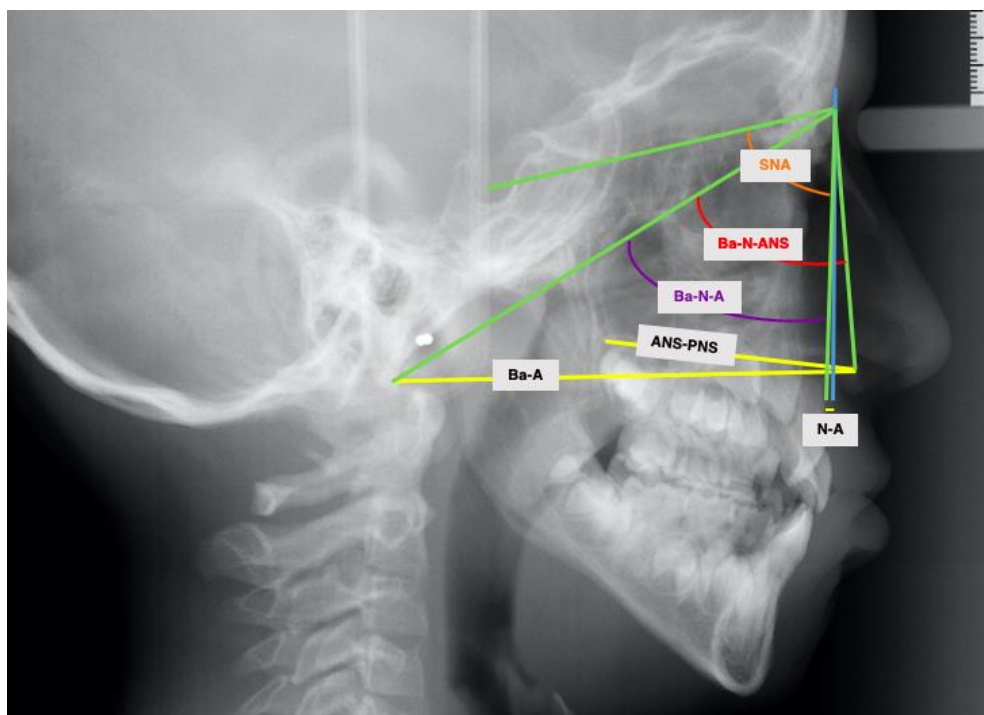


Figure 14: Maxillary cephalometric measurements.

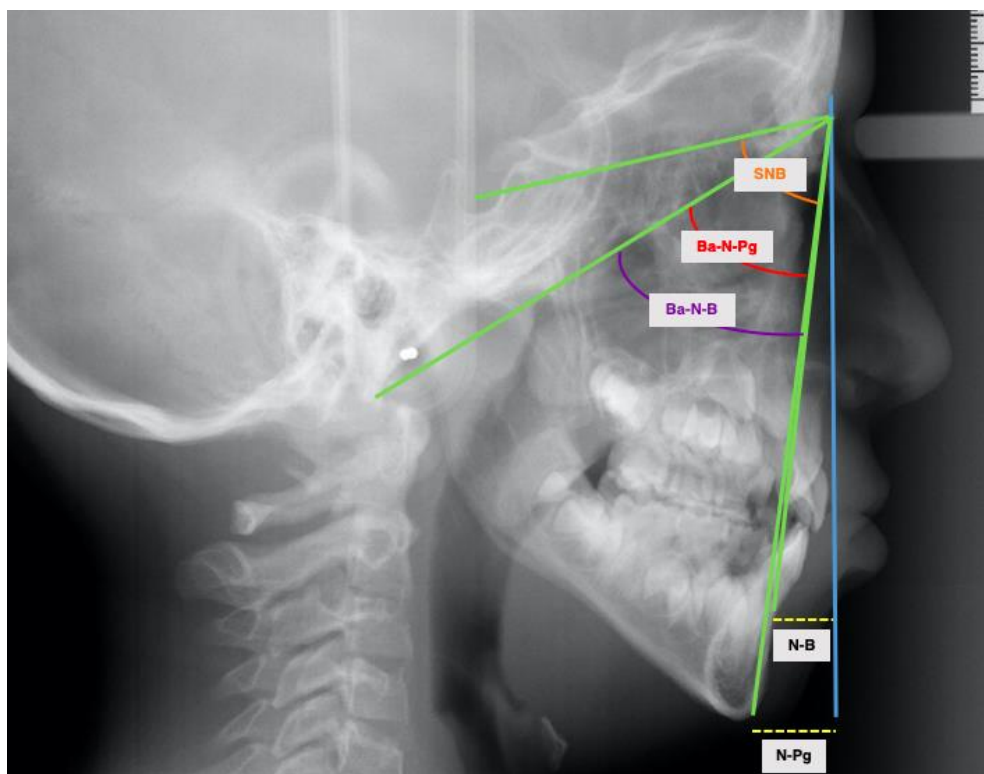


Figure 15: Mandibular cephalometric measurements.

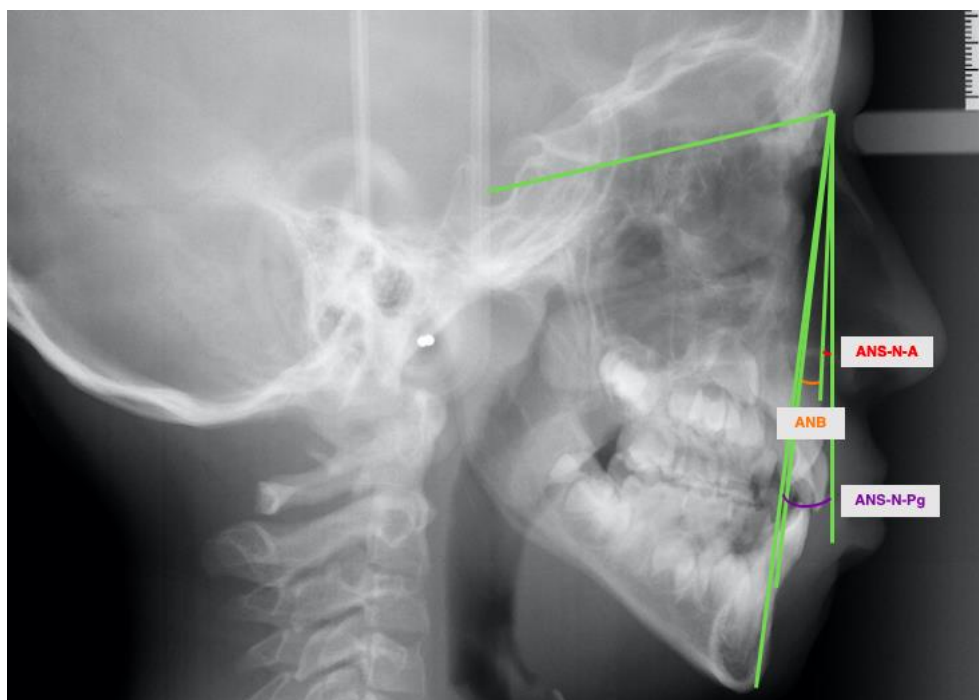


Figure 16: Dento-alveolar cephalometric measurements.



Figure 17: Vertical facial growth cephalometric measurements.

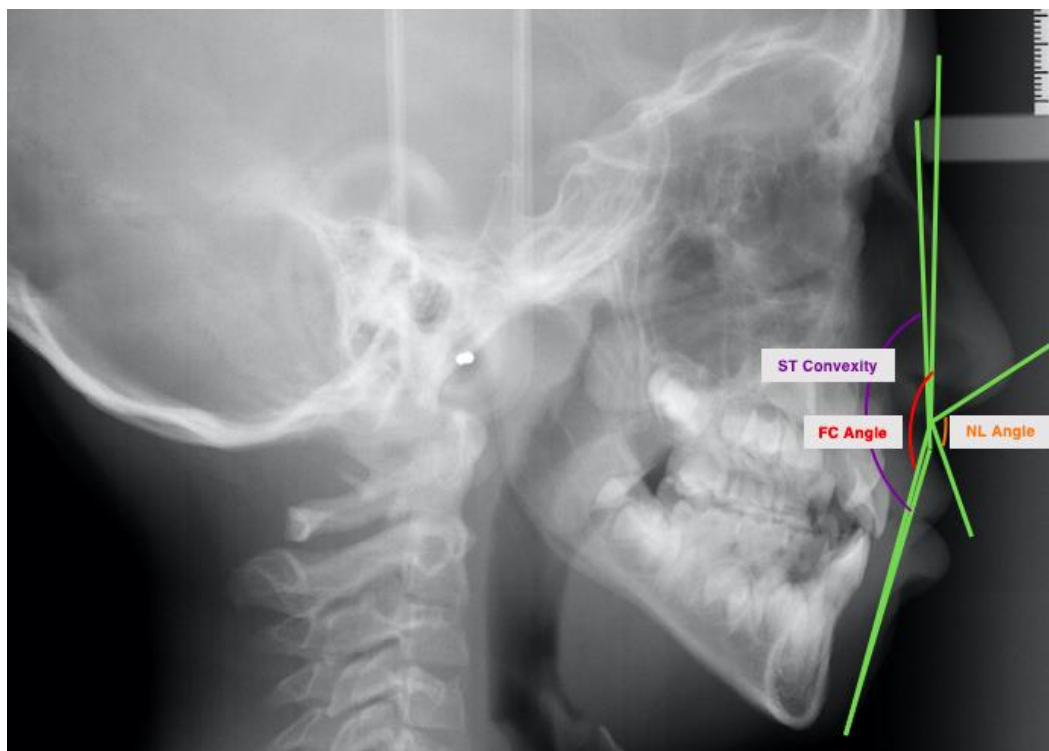


Figure 18: Soft tissue cephalometric measurements.

1.12.7 Facial Growth in Cleft Lip & Palate

Differences in facial morphology in patients with cleft lip and palate compared to patients without a cleft include (1) shortened maxilla and mandible, (2) reduced posterior maxilla height and increased width, (3) reduced palate size, oropharynx and pharyngeal depth, (4) reduced posterior mandible height, (5) bimaxillary retrognathia, (6) inferior position of hyoid, (7) reduced tongue height and velar length, (8) reduced nasolabial angle, (9) reduced percent nose, and (10) reduced mandibular incisor projection and inclination (84,86–89). There does not appear to be any difference in skull base anatomy between patients with and without cleft palate (90,91).

Patients with larger alveolar gaps have been shown to have poorer maxillary protrusion and length (84,92). It has previously been shown in patients with cleft lip and palate that overall midface growth in patients that do not undergo lip or palate repair is similar to patients without any cleft. This finding has led to the conclusion that surgical intervention does cause a growth disturbance (7). Liao et al. have shown that when compared to patients who received lip repair only, palate repair leads to limited anteroposterior development of the maxilla, and decreased forward displacement (93). Several other studies have shown similar outcomes in regards to the effect of palate repair on maxillary growth (21,23). Several studies have shown that pressure from the lip repair can cause the upper anterior teeth to become retroclined, leading to an anterior crossbite (7,94–97).

1.13 THESIS RATIONALE

The use of PSO devices in the management of patients with CL/P remains controversial. In addition, few research studies actually compare patient outcomes achieved by different types of PSO devices (35). To date, limited research has compared long-term facial growth, dental occlusion, and nasolabial aesthetics between patients who received an active PSO device versus a passive PSO device. The research that does exist on this topic is limited by small patient cohorts with multiple surgeons and management protocols within the same experimental group (35,98). At our institution we have a single surgeon that has been using active and passive PSO devices for over 15 years. All of these patients receive the same operative and non-operative cleft management, except for the PSO device used. This presents us with the unique opportunity to examine outcomes in a single surgeon's cohort of patients over a long-term period. By using a cohort of patients operated on by a single surgeon with the same management protocol we can eliminate some of the unnecessary confounding variables which are present in the majority of current cleft palate literature (35,98).

Both active and passive PSO devices have their strengths and weaknesses. Passive devices have an increased burden of care on the patient's families because they require weekly device adjustments. Active PSO devices require fewer follow-up visits, but have the added risk and cost associated with operative insertion of the device. With steps towards reducing unnecessary procedures, risks, and costs in the medical system, it is important to determine whether one type of PSO device produces superior results. The results from this thesis will be important for determining management of patients with CL/P moving forward. Overall, this work will give a more conclusive answer about the effects of the PSO devices on nasolabial aesthetics, dental occlusion, and facial growth. In addition, this will be the first study of its nature to compare outcomes in patients that received an active versus a passive device.

1.14 RESEARCH OBJECTIVES AND HYPOTHESIS

There are 4 principle objectives to this research:

- 1) Perform a systematic review of current literature describing the long-term effects of different PSO devices used for the management of cleft palate.
- 2) Evaluate and compare the nasolabial aesthetic changes in patients who were treated with an active PSO device, passive PSO device, or no PSO device at 1 year, 5 years, and 10 years.
- 3) Evaluate and compare dentoalveolar development/occlusion in patients who were treated with an active or passive PSO device at 5 years and 10 years.
- 4) Evaluate and compare the facial growth in patients who were treated with an active or passive PSO device at 5 years and 10 years.

We hypothesize that nasolabial aesthetics, dentoalveolar development, and facial growth will be comparable between patients that received active PSO devices and passive PSO devices. We hypothesize that active and passive PSO devices will make nasolabial aesthetics in patients with larger alveolar gaps comparable to patients who had smaller gaps and did not require a PSO.

Chapter 2: Systematic Review of the Literature on the Long-term Patient Outcomes Associated with Pre-Surgical Orthopedic Devices

The use of pre-surgical orthopedic devices in cleft lip/palate patients is controversial. The literature that exists on this topic is extremely varied. The purpose of this chapter is to outline the current state of knowledge of the long-term outcomes of patients with cleft lip/palate treated with pre-surgical devices prior to lip repair.

1.1 INTRODUCTION

Clinical use of active and passive presurgical orthopedic (PSO) devices for the management of patients with cleft lip/palate is a controversial topic. It is widely accepted that these devices are useful for decreasing alveolar gap size prior to lip repair (99–102), but their long-term effects on nasolabial aesthetics, dental occlusion, and facial growth are still debated (35,54,103–108). Consequently, the use of these devices is dependent on surgeon experience and caregiver preference (30).

To date, there is a large body of research examining the outcomes of patients treated with PSO devices, but there is no consensus on their effect on long-term patient outcomes (35,98). The lack of consensus on the use of these devices is likely in part due to the quality of the research itself. Research in cleft lip and palate is often limited by small sample sizes and variable management protocols. Frequently, patients from numerous sites and surgeons are included in a single study to try and increase the study cohort. While advantageous for increasing the power of studies, grouping patients undergoing dissimilar management ultimately creates confounding factors within the studies (e.g. surgeon experience, surgical procedure) (35,102,109). The variability that exists within and in between comparison groups creates bias and confusion when drawing conclusions from the research performed. In addition, there is also a paucity of research actually comparing the difference in outcomes between patients treated with different types of PSO devices (35).

The primary purpose of the research in this chapter was to complete a systematic review of the literature pertaining to the use of PSO devices in cleft lip/palate and their effect on long-term patient outcomes.

1.2 METHODOLOGY

A comprehensive literature review of Embase and Ovid databases was performed to identify all English-language publications related to unilateral cleft palate, presurgical devices, and patient outcomes. Selection criteria for included studies were as follows:

Inclusion criteria:

- Describe the use of PSO for unilateral cleft palate management
- Describe patient outcomes past removal of device
- Include human subjects
- English-language articles
- Published at any date
- Any study design, including case series (>10 cases)

Exclusion criteria:

- Do not describe the use of PSO for cleft management
- Do not describe patient outcomes past removal of device
- Control group is patients without a cleft lip/palate
- Did not separate unilateral and bilateral cleft outcomes
- Study designed to validate a small modification of a previously validated device
- Case report (<10 cases)
- Non-original studies

Key search terms included: “cleft lip”, “cleft palate”, “preoperative care”, “orthodontics”, “palatal obturators”, and “infant”. An academic librarian was involved to help build the literature search. All of the abstracts were reviewed independently by two reviewers. Any disagreement about the inclusion of a study was resolved by consensus. In addition, the reference lists of the included articles were hand-searched for any articles missing from the database search. Following

the full-article review, a total of 41 articles were included in this systematic review. Figure 19 describes the process of inclusion and exclusion of articles in this study.

The following data was collected for each paper: (1) study title, (2) authors, (3) year of publication, (4) journal of publication, (5) type of publication, (6) number of patients included in study, (7) type of PSO device used, (8) whether patient management protocols were standardized within and between groups, (9) outcomes measured, (10) age of patients at analysis, and (11) conclusions drawn about the device being evaluated. Meta-analysis was not performed due to the heterogeneity of reported results.

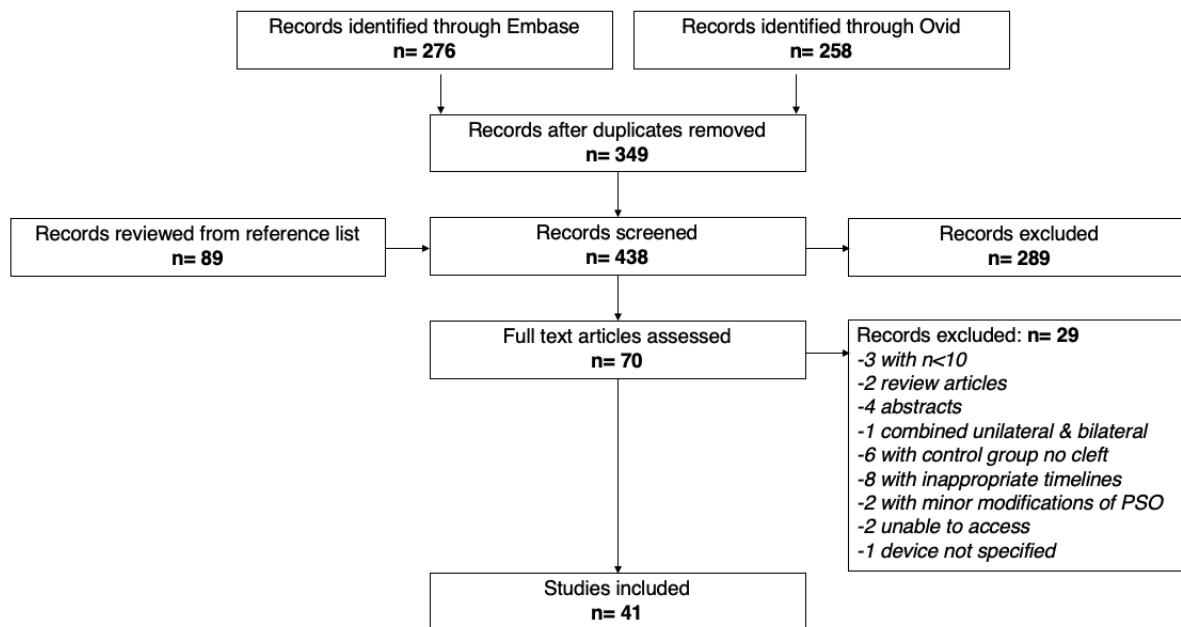


Figure 19: Flowchart of study inclusion.

1.3 RESULTS

The literature search yielded a total of 438 studies to review, of which 41 studies met criteria for inclusion in the systematic review (35,45,46,51,54–58,101,103,107,108,110–136). Of the 41 studies, 30 were retrospective studies and 11 were prospective studies. See Table 2 for the list of all included articles, year of publication, and type of study.

On average, studies had a total of 32.9 patients per intervention group. Sixteen articles examined outcomes in patients under 5 years of age, 25 articles for patients 5 to 10 years old, and 4 articles for patients over 10 years old. Of the 41 research articles, 23 focused on passive devices, 8 on active devices, and 10 compared active and passive devices. In total, 13 articles described nasolabial aesthetics, 9 described facial growth, 23 described dental arch/occlusion outcomes, 1 described rates of revision surgeries, and 1 described changes in airway anatomy. For articles reporting on dental arch outcomes, 22% reported that the PSO device improved dental arch/occlusion, 22% reported that the PSO device caused worse dental arch/occlusion, and 56% reported no difference in outcomes between patients that had a PSO device compared to those that did not (Figure 20). For articles reporting on nasolabial aesthetic outcomes, 64% reported improvement in nasolabial aesthetics with the use of a PSO device and 36% reported no difference in outcomes between patients that did have a PSO device compared to those that did not (Figure 20). For articles reporting on facial growth outcomes, 33% of studies reported that PSO devices worsened facial growth and 67% reported no difference in outcomes between patients that did have a PSO device compared to those that did not (Figure 20). The sole article reporting on airway measurements described no difference in outcomes between patients that did have a PSO device compared to those that did not. The sole article reporting on rates of revision surgery described a reduced number of revision surgeries in patients that had a PSO device (Figure 20).

A total of 11 articles examined a patient cohort from a single surgeon's practice, 21 used a cohort from multiple sites and/or surgeons, and 9 examined a cohort from one site with an unspecified number of surgeons involved in the care of the patients. Consistency in management protocols was quite variable between these 3 groups (Figure 21). Variability in the protocols included different operating surgeons (73%), different type and timing of lip and/or palate repair (41%), whether or not patients received GPP (10%), and whether patients received revision surgeries (17%). Seven percent of papers did not describe their management protocols and 9% described similar management for lip repair but did not describe management following lip repair. In total, 15% of papers had a consistent management protocol within and in between experimental groups.

With respect to the 11 articles that investigated a single surgeon's practice, 8 articles examined the effects of a passive device and 3 examined the effects of an active device. Three articles reported on nasolabial aesthetics, 3 reported on dental arch/occlusion, 1 reported on facial growth, 1 reported on dental arch/occlusion and growth, 2 articles reported on dental arch/occlusion and nasolabial aesthetics, and 1 article compared rates of revision surgeries. Six of the 11 (55%) single-surgeon articles had inconsistent management protocols for all of their patients or did not specify whether the management between the control and experimental groups was the same. In the 5 articles that described consistent management protocols between groups, no study specified whether the treatment/control groups differed in their management following lip repair (e.g. palate surgery, revision surgeries etc.). Two of the 5 articles examined outcomes up to 4 to 6 months of age and the 3 remaining articles measured outcomes each at one time point between 1 to 10 years of age. On average, these articles had 19.8 (range 13 to 42) patients in the experimental group and 29.5 (range 5 to 61) patients in the control group. Three articles reported improved nasolabial aesthetics with the use of a PSO device, 1 article reported no difference in nasolabial aesthetics whether or not a PSO device was used, and 1 article reported no difference in dental arch measurements whether or not a PSO device was used.

Paper	Authors	Journal	Year	Type of Publication
1 Effect of Presurgical Nasoalveolar Molding on Nasal Symmetry in Unilateral Complete Cleft Lip/Palate Patients after Primary Cheiloplasty without Concomitant Nasal Cartilage Dissection: Early Childhood Evaluation.	Liang Z, et al.	Cleft Palate-Craniofacial Journal	2018	Retrospective cohort
2 Active presurgical infant orthopedics for unilateral cleft lip and palate: Intercenter outcome comparison of Latham, modified McNeil, and nasoalveolar molding.	Kornbluth M, et al.	Cleft Palate-Craniofacial Journal	2018	Retrospective cohort
3 Midface Growth in Patients With Unilateral Cleft Lip and Palate Treated With a Nasoalveolar Molding Protocol.	Rubin M.S, et al.	The Journal of Craniofacial Surgery	2019	Retrospective cohort
4 The effect of nasoalveolar molding on nasal airway anatomy: A 9-year follow-up of patients with unilateral cleft lip and palate.	Massie J.P, et al.	Cleft Palate-Craniofacial Journal	2018	Retrospective cohort
5 Burden of care of various infant orthopedic protocols for improvement of nasolabial esthetics in patients with CUCLP.	Singer E, et al.	Cleft Palate-Craniofacial Journal	2018	Retrospective cohort
6 Long-term effect of presurgical nasoalveolar molding on growth of maxillary arch in unilateral cleft lip and palate: randomized controlled trial.	Shetty V, et al.	International Journal of Oral and Maxillofacial Surgery	2017	Randomized controlled trial
7 A Comparison of Mixed Dentition Dental Development in Cleft Patients Treated With and Without the Latham-type Appliance.	Lin J, et al.	Pediatric Dentistry	2017	Retrospective cohort
8 Comparison of two treatment protocols in children with unilateral complete cleft lip and palate: Tridimensional evaluation of the maxillary dental arch.	Jorge P.K, et al.	Journal of Cranio-Maxillofacial Surgery	2016	Retrospective cohort
9 Comparison of Early Onset Nasoalveolar Molding with Patients Who Presented for Molding Up to 1 Year of Age.	Shetty V, et al.	Journal of Oral and Maxillofacial Surgery	2016	Randomized controlled trial
10 Surgeon's and Caregivers' Appraisals of Primary Cleft Lip Treatment with and without Nasoalveolar Molding: A Prospective Multicenter Pilot Study.	Broder H.L, et al.	Plastic and reconstructive Surgery	2016	Non-randomized clinical trial
11 Presurgical orthopedics has no effect on archform in unilateral cleft lip and palate.	Adali N, et al.	Cleft Palate-Craniofacial Journal	2012	Non-randomized clinical trial
12 Presurgical nasoalveolar molding orthopedic treatment improves the	Sasaki H, et al.	Journal of Craniofacial Surgery	2012	Retrospective cohort

outcome of primary cheiloplasty of unilateral complete cleft lip and palate, as assessed by naris morphology and cleft gap.

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|----|---|-------------------------|------------------------------------|----------------------------------|
| 13 | Long-term treatment outcome of presurgical nasoalveolar molding in patients with unilateral cleft lip and palate. | Clark S.L, et al. | Journal of Craniofacial Surgery | 2011 Retrospective cohort |
| 14 | Nasoalveolar molding improves long-term nasal symmetry in complete unilateral cleft lip-cleft palate patients. | Barillas I, et al. | Plastic and Reconstructive Surgery | 2009 Retrospective cohort |
| 15 | Infant orthopedics and facial growth in complete unilateral cleft lip and palate until six years of age (Dutchcleft). | Bongaarts C.A.M, et al. | Cleft Palate-Craniofacial Journal | 2009 Randomized controlled trial |
| 16 | Effect of infant orthopedics on facial appearance of toddlers with complete unilateral cleft lip and palate (Dutchcleft). | Bongaarts C.A.M, et al. | Cleft Palate-Craniofacial Journal | 2008 Randomized controlled trial |
| 17 | Infant orthopedics has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). | Bongaarts C.A.M, et al. | Cleft Palate-Craniofacial Journal | 2006 Randomized controlled trial |
| 18 | Infant orthopedics and facial appearance: A randomized clinical trial (Dutchcleft). | Prahl C, et al. | Cleft Palate-Craniofacial Journal | 2006 Randomized controlled trial |
| 19 | The effect of infant orthopedics on the occlusion of the deciduous dentition in children with complete unilateral cleft lip and palate (Dutchcleft). | Bongaarts C.A.M, et al. | Cleft Palate-Craniofacial Journal | 2004 Randomized controlled trial |
| 20 | The effects of active infant orthopedics on occlusal relationships in unilateral complete cleft lip and palate. | Chan K.T, et al. | Cleft Palate-Craniofacial Journal | 2003 Retrospective cohort |
| 21 | A randomized prospective clinical trial of the effect of infant orthopedics in unilateral cleft lip and palate: Prevention of collapse of the alveolar segments (Dutchcleft). | Prahl C, et al. | Cleft Palate-Craniofacial Journal | 2003 Randomized controlled trial |
| 22 | A randomised prospective clinical trial into the effect of infant orthopaedics on maxillary arch dimensions in unilateral cleft lip and palate (Dutchcleft). | Prahl C, et al. | European Journal of Oral Sciences | 2001 Randomized controlled trial |
| 23 | Comparison between palatal configurations in UCLP infants with and without a Hotz plate until four years of age. | Mishima K, et al. | Cleft Palate-Craniofacial Journal | 2000 Retrospective cohort |
| 24 | Quantitative 3D maxillary arch evaluation of two different infant managements for unilateral cleft lip and palate. | Prasad C.N, et al. | Cleft Palate-Craniofacial Journal | 2000 Retrospective cohort |
| 25 | Cleft lip and palate treated by presurgical orthopedics, gingivoperiosteoplasty, and lip adhesion (POPLA) compared with | Millard D.R, et al. | Plastic and Reconstructive Surgery | 1999 Retrospective cohort |

previous lip adhesion method: A preliminary study of serial dental casts.

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|----|--|------------------------------|---|---------------------------|
| 26 | Changes produced by presurgical orthopedic treatment before cheiloplasty in cleft lip and palate patients. | Kozelj V | Cleft Palate-
Craniofacial Journal | 1999 Retrospective cohort |
| 27 | Analysis of primary gingivoperiosteoplasty in alveolar cleft repair. Part I: Facial growth. | Henkel K.-O, et al. | Journal of Cranio-
Maxillo-Facial
Surgery | 1997 Retrospective cohort |
| 28 | Morphologic effect of preoperative maxillofacial orthopedics (T-traction) on the maxilla in unilateral cleft lip and palate patients. | Larson M, et al. | Cleft Palate-
Craniofacial Journal | 1993 Retrospective cohort |
| 29 | Craniofacial development in children with unilateral cleft of the lip, alveolus, and palate treated according to three different regimes. Assessment of nasolabial appearance. | Brattstrom V, et al. | Scandinavian
Journal of Plastic
and Reconstructive
Surgery and Hand
Surgery | 1992 Retrospective cohort |
| 30 | Early bone grafting in complete cleft lip and palate cases following maxillofacial orthopedics. III. A study of the dental occlusion. | Larson O, et al. | Scandinavian
Journal of Plastic
and Reconstructive
Surgery | 1983 Retrospective cohort |
| 31 | An Intercenter Comparison of Dental Arch Relationships and Craniofacial Form Including a Center Using Nasoalveolar Molding. | Peanchitlertkajorn S, et al. | Cleft Palate—
Craniofacial Journal | 2018 Retrospective cohort |
| 32 | Presurgical Nasoalveolar Molding for Correction of Cleft Lip Nasal Deformity: Experience From Northern India | Mishra, et al. | Open Access Journal
of Plastic Surgery | 2010 Retrospective cohort |
| 33 | A Six-Center International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 4. Assessment of Nasolabial Appearance | Asher-McDade, et al. | Cleft Palate—
Craniofacial Journal | 1992 Retrospective cohort |
| 34 | A Six-Center International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 3. Dental Arch Relationships | Mars, et al. | Cleft Palate—
Craniofacial Journal | 1992 Retrospective cohort |
| 35 | Comparative Study of Early Secondary Nasal Revisions and Costs in Patients With Clefts Treated With and Without Nasoalveolar Molding | Patel, et al. | Journal of
Craniofacial Surgery | 2015 Retrospective cohort |
| 36 | The Eurocleft Study: Intercenter Study of Treatment Outcome in Patients With Complete Cleft Lip and Palate. Part 2: Craniofacial Form and Nasolabial Appearance | Brattstrom, et al. | Cleft Palate—
Craniofacial Journal | 2005 Retrospective cohort |

37	Postoperative Nasal Forms After Presurgical Nasoalveolar Molding Followed by Medial-Upward Advancement of Nasolabial Components With Vestibular Expansion for Children With Unilateral Complete Cleft Lip and Palate	Nakamura, et al.	Journal of Oral and Maxillofacial Surgery	2009 Retrospective cohort
38	The Americleft Study: An Inter-Center Study of Treatment Outcomes for Patients with Unilateral Cleft Lip and Palate Part 3. Analysis of Craniofacial Form	Daskalogiannakis, et al.	Cleft Palate—Craniofacial Journal	2011 Retrospective cohort
39	The Americleft Study: An Inter-Center Study of Treatment Outcomes for Patients with Unilateral Cleft Lip and Palate Part 2. Dental Arch Relationships	Hathaway, et al.	Cleft Palate—Craniofacial Journal	2011 Retrospective cohort
40	A Six-Center International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 2. Craniofacial Form and Soft Tissue Profile	Molsted, et al.	Cleft Palate—Craniofacial Journal	1992 Retrospective cohort
41	The Eurocleft Study: Intercenter Study of Treatment Outcome in Patients with Complete Cleft Lip and Palate. Part 3: Dental Arch Relationships	Molsted, et al.	Cleft Palate—Craniofacial Journal	2005 Retrospective cohort

Table 2: Summary of articles included in final systematic review.

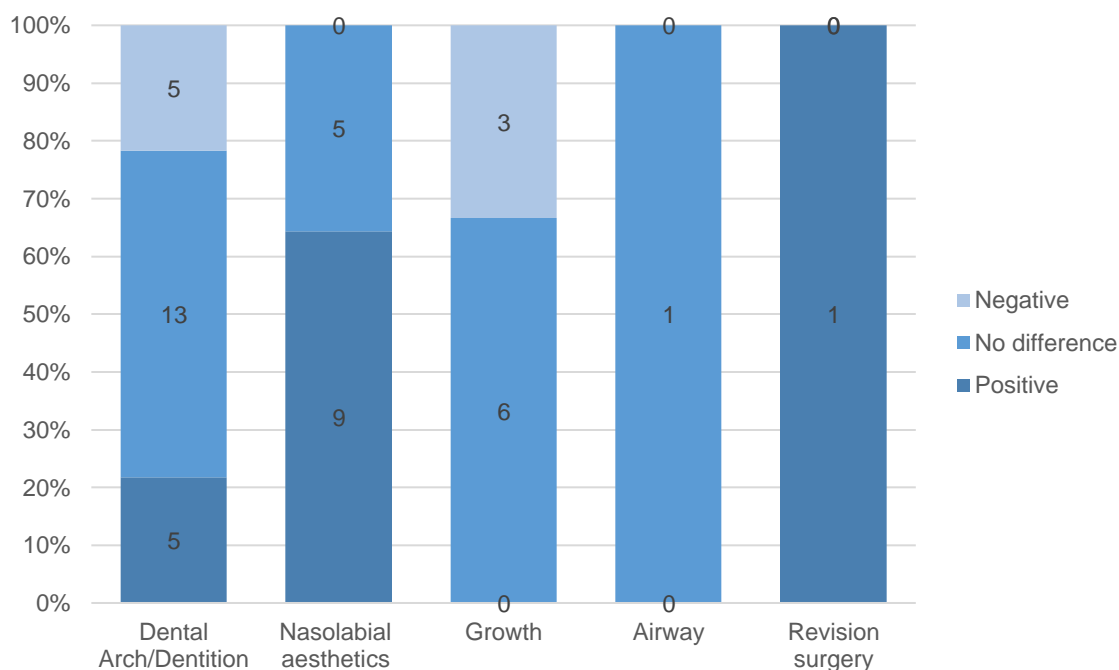


Figure 20: Distribution of results in all articles. Positive result indicates that PSO device improved outcomes compared to no device and negative indicates PSO device worsened outcomes.

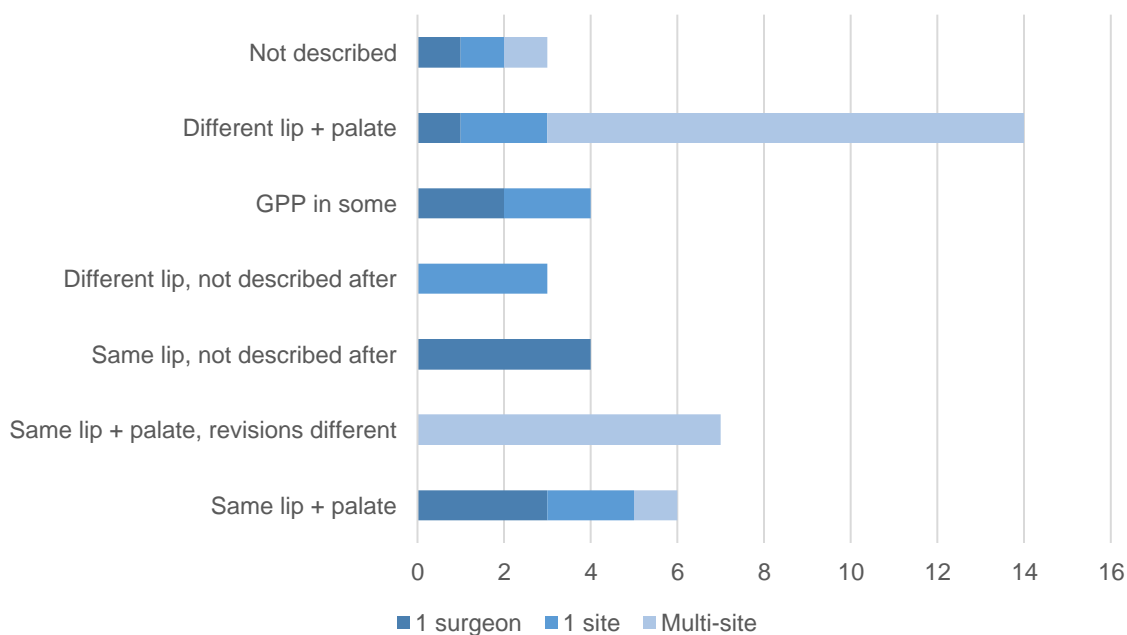


Figure 21: Types of variability in the methodology of the reviewed studies.

1.4 DISCUSSION

Overall, this systematic review identified 41 studies examining the long-term effects of PSO device use. The primary objective of this systematic review was to describe the current literature on the long-term outcomes of patients treated with PSO devices. To this effect, the main clinical outcomes measured in these studies were nasolabial aesthetics, facial growth, and dental arch/occlusion. Overall, 31% found improved outcomes with PSO devices, 17% showed worse outcomes with PSO devices, and 52% found no difference in outcomes in patient treated with a PSO device versus no device. This large discrepancy between studies highlights the lack of consensus on the long-term effects of PSO device use in patients with cleft lip/palate.

A potential reason for the discrepancy found in this systematic review is the large variability in management of the patients in these studies. This variability in management within experimental groups creates many confounding factors that make it difficult to draw meaningful conclusions from the results. Variability in patient management has previously been identified as weaknesses in cleft lip/palate literature but have never been quantified as was done in this review (35,102). In total, this review identified only 7.3% of papers had uniform management protocols between and within comparison groups.

Identified sources of variability in patient management included different operating surgeons, different timing/type of lip and/or palate repair, different patients receiving GPP, and patients receiving different types of revision surgeries. These differences in management protocols are especially apparent in the Eurocleft studies, Americleft studies, and the Dutchcleft studies (55,56,117–120,101,110–116). These large cohort studies were some of the earliest studies describing nasolabial aesthetic, dental occlusion, and facial growth outcomes in patients with cleft palate that received PSO device treatment. Each of these studies compared patients from 4 to 6 centres that all differed in the PSO device used (active versus

passive), type/timing of lip and palate surgery, and the surgeon that operated on the patients. Differing times of lip and palate repair essentially nullifies any comparison that can be drawn between the PSO groups because the age of the repair has been previously shown to affect growth (24–26). In addition, in all of these studies the comparison groups were each operated on by different surgeons. It cannot be excluded that the reported results may be a consequence of the operating surgeon and not the PSO device used (121). Despite being large trials, the variability in patient management makes it difficult to isolate and conclude how the PSO devices influenced patient outcomes.

In an effort to eliminate some potential bias, this review also focused on studies from a single surgeon's practice however, multiple confounding factors and methodology flaws were still identified. The review identified a total of 11 single surgeon studies from which 6 studies still had inconsistent management protocols between groups. In total, 5 single-surgeon studies had consistent management protocols up to the time of lip repair (57,103,121,125,137). These studies eliminated many confounding variables, but still had several weaknesses that decreased the validity of their results. All 5 studies did not report on the number of patients requiring further surgeries following palate repair. This is an important distinction that must be made when evaluating patients long-term; changes in clinical outcomes could be attributed to their revision surgeries instead of their initial management. These 5 studies were also weakened by short follow-up times or selection bias as described below.

The 2018 paper by Liang et al. reported no overall difference in nasolabial aesthetics between patients that received a passive PSO device and no device. The strengths of this study were the consistent management protocol for each patient group, and the long-term (5-year) follow-up period. Unfortunately, this study did not comment on initial alveolar gap size/severity in the patient groups, which means that selection bias cannot be excluded. It is difficult to draw conclusions from this study without knowing if these patient cohorts started with similar alveolar

gap sizes. The 2011 study by Clark et al. focused on dental occlusion and nasolabial aesthetic analysis using 3-dimensional molds and photographs. This study showed no difference in occlusion or nasolabial aesthetic outcomes in patients treated with a passive PSO versus no PSO. The 2009 study by Barillas et al. was a single-surgeon study with a 9-year follow-up interval comparing nasal outcomes in patients treated with a passive device versus no device. This study found that passive devices improved nasal symmetry. The strengths and weaknesses of the Clark et al. and Barillas et al. studies were similar to the Liang et al. paper. The last two single-surgeon studies were by Adali et al. and Sasaki et al., both of which had follow-up periods that were less than 1 year of age. Adali et al. looked at the effect of an active PSO device on dental arch up to 6 months of age and found no difference between patients treated with an active device versus no device. The 2012 study by Sasaki et al. examined nasolabial aesthetics up to 4 months of age and found improvement with passive device treatment. Overall, the main weakness of these final 2 single-surgeon studies was the short-term follow-up. These studies were less informative because they did not examine the changes that can occur with growth and dental development (98).

This is the second retrospective review to outline long-term outcomes in patients with cleft lip/palate after the use of PSO devices. The first retrospective review on this subject examined prospective trials looking at long-term outcomes following PSO device use (98). This review excluded all retrospective studies and identified a total of 12 prospective studies. This study concluded that passive devices have no positive effect on motherhood satisfaction, feeding, speech, facial growth, dental arch, occlusion, and nasolabial aesthetics and active devices have no positive effects on feeding (98). Overall, the Uzel et al. review was the first to summarize long-term patient outcomes from PSO device use but was limited by the exclusion of retrospective studies. Retrospective studies form a large proportion of cleft palate literature, our review suggests 73% of cleft palate literature is retrospective in nature. Excluding retrospective studies in this field significantly limits the studies that can be examined. With our more recent review

(2019 versus 2011) and inclusion of retrospective studies, this second review is a more thorough and up to date systematic review than the original review done in 2011 (98). Despite differences in the inclusion criteria of both systematic reviews, the overall results are similar. There is no definite conclusion on the long-term outcomes in patients that have received PSO treatment. Some studies identified detriments to growth, nasolabial aesthetics and dental arch/occlusion while others identified no effect or positive effects.

1.5 CONCLUSION

Research in the field of cleft lip and palate is greatly limited by small sample sizes and confounding factors such as multi-surgeon cohorts with multiple different protocols for patient management. This review has further highlighted the variability that exists in cleft palate literature. In regard to the long-term effects of PSO devices, there still remains no consensus on this subject. This lack of consensus is likely due to the multitude of confounding factors that influence the reported outcomes. In addition, there are very few studies actually comparing different types of PSO devices. The studies that do exist are also limited by methodological flaws. Moving forward, further research comparing active and passive PSO devices is warranted. In addition, confounding factors need to be eliminated from the comparison groups so that control and experimental groups are uniform in the way they are managed. Finally, these studies should match patients between treatment groups based on cleft severity. This would improve reliability of the research and resolve the differing conclusions as to how PSO devices affect long-term facial growth, dental arch development, and nasolabial aesthetics.

Chapter 3: 10-Year Nasolabial Aesthetic Comparison in Patients with Different Pre-surgical Orthopedic Devices

Long-term outcomes in patients with cleft palate that are treated with different pre-surgical orthopedic devices are still highly debated. There is no consensus in the literature about the long-term effects of these devices on nasolabial aesthetics, and there is minimal research comparing the effects of different types of devices. The purpose of this chapter was to evaluate the 10-year nasolabial aesthetic outcomes in patients treated with active or passive pre-surgical orthopedic devices and patients treated with no device.

1.1 INTRODUCTION

The management of patients with cleft lip and palate (CL/P) is a multi-staged, multi-disciplinary process (34). The overall objective of treating patients with CL/P is to give them a functional lip and palate with good aesthetic results (32,33). Pre-surgical orthopedic (PSO) devices are a possible management option used to decrease the size of the alveolar gap, but have also been shown to possibly improve aesthetic outcomes (52). Pre-surgical orthopedic devices can be active or passive. Active PSO devices consist of a pin-retained appliance that is adjusted daily to drive the edges of the alveolar gap closer together, whereas passive devices are gradually molded to bring the respective nasal and alveolar elements closer together (35).

A significant reported benefit of PSO device use is improved nasolabial aesthetics (52). Several studies have shown improved nasolabial aesthetics with active and passive devices compared to patients who did not receive PSO device treatment (35,51,52,128). Specifically, passive devices have been shown to improve alar base symmetry, vermillion symmetry, and columellar lengthening/deviation (138,139). While studies have shown that active devices have positive effects on overall nasolabial aesthetics, no specific effects have been described (35). Conversely, there are also studies that show no improvement in nasolabial aesthetics with the use of a PSO device (103,116). Ultimately, there is no consensus in the literature about the effect of PSO devices on nasolabial aesthetics.

In addition to a lack of consensus on the specific effects of PSO devices on nasolabial aesthetics, the research that is published on this subject is limited by small sample sizes and confounding factors that limit the generalizability of the results (35,52,102,109). Confounding factors include multiple operating surgeons, different surgical protocols, different rates of revision surgery, and varying degrees of cleft severity between comparison groups. These confounding factors make it

difficult to draw conclusions about the effects of the PSO device on nasolabial aesthetics. In addition to a lack of consensus on the effect of PSO devices on nasolabial outcomes, there are few studies comparing the long-term patient outcomes between patients treated with different types of PSO devices (35). These studies are limited because centres often do not use both active and passive devices, so the outcomes are rarely compared.

In conclusion, a study comparing the long-term effects of active and passive PSO devices on nasolabial aesthetics is required. The objective of this research chapter was to compare nasolabial aesthetic outcomes in patients from a single surgeon's cohort treated with an active PSO device, passive PSO device, or no device over a 10-year period.

1.2 METHODOLOGY

All patients in this study were treated by a cleft palate team that has a single cleft palate surgeon, a single orthodontist, and a single speech language pathologist involved in the care of every patient. At our institution patients and their families are offered treatment with a PSO device at approximately 2 weeks of age if their alveolar gap is greater than 4mm. The decision as to whether an active or a passive device is used is based on caregiver preference and capacity to manage the device. Patients undergo a modified Mohler lip repair at approximately 3 months and a palatoplasty at approximately 12 months. Patients and their families are also offered lip revision surgery if either the surgeon or caregiver are concerned about the aesthetics or functionality of the lip repair. Lip revision surgery is offered at any time during management and involves a total takedown and redo of the lip repair.

A retrospective review of all patients with cleft lip and palate in a single surgeon's practice from 2002-2018 was performed. All patients with a unilateral complete or incomplete cleft of the primary palate were identified. Patients were excluded if they had a known syndrome, bilateral cleft lip or palate, or were not operated on by the primary surgeon. Patients were divided into 3 groups based on whether they received pre-surgical care with an active PSO device, a passive PSO device, or no PSO device. The following basic patient demographic information was collected through a chart review: (1) involvement of primary and secondary palate, (2) side of cleft, (3) smoking mother, (4) family history of cleft lip or palate, (5) use of pre-surgical taping, (6) age of active device insertion (if applicable), (7) age of lip and palate repair, (8) type of lip and palate repair, and (9) lip revision surgery.

Initial patient measurements including anterior vertical alveolar gap (AG), anterior horizontal AG, palate width at the level of the posterior hard palate, cleft width at the level of the posterior hard palate, and bilateral alar base measurements were recorded (Figure 22). These measurements were recorded at 3 time points: device

insertion, lip repair, and palate repair. Patients with no device did not have measurements taken until the time of lip repair. Patients with a device had their initial measurements performed on plaster molds that are taken intra-orally at the time of their initial visit. These molds were measured by a single blinded reviewer using electronic calipers to the nearest 1/100 of a millimeter. Measurements were repeated on 10 patients at 3 separate occasions within 1 month to measure intra-rater reliability. Alar base measurements were recorded only at the time of lip repair and posterior palate/cleft width were recorded only at the time of palate repair. Measurements at the time of lip and palate repair are recorded intra-operatively by the primary surgeon using calipers (to the nearest 1/10 of a millimeter) and are recorded in the patient chart. No intra-rater reliability measurements were performed on the surgeon's measurements as they were considered to be the standard for measurements.

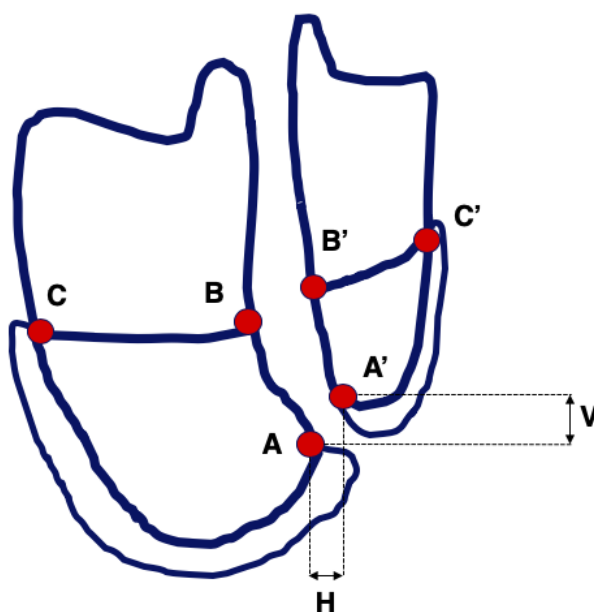


Figure 22: Recorded cleft palate landmarks. A/A': antero-medial edge of hard palate (non-cleft and cleft side); B/B': postero-medial edge of hard palate (non-cleft and cleft side); C/C': postero-lateral edge of hard palate (non-cleft and cleft side); V: vertical alveolar gap; H: horizontal alveolar gap.

1.3 Nasolabial Aesthetics

Photographs are taken at every patient follow-up visit and kept in patient charts. Patient photographs were digitized and evaluated by a single blinded reviewer. Worms view and frontal view photographs were used for analysis. All photographs were cropped to show only the patient's nose and lips. All other facial features were excluded. Each photograph was evaluated using a validated 11-point scale (**APPENDIX 2- NASOLABIAL AESTHETIC RATING SCALE**). Features evaluated in the nasolabial scale included: (1) nasal tip symmetry, (2) nostril circumference, (3) nostril rim symmetry, (4) recurvatum of nostril, (5) columella angulation, (6) Cupid's Bow, (7) vermillo-cutaneous junction, (8) vermillo-mucosal junction, (9) alar base symmetry, (10) scar position, and (11) scar quality (Figure 7). Each specific nasolabial feature was graded as "favorable" or "unfavorable". If the rater was unable to determine whether the result was favorable or unfavorable the section was left blank and excluded from analysis. A subset of 20 randomly selected photographs were analysed a total of 3 separate times over the course of 1 month to calculate intra-rater reliability.

1.3.1 Statistical Analysis

For comparing demographic information, chi square tests were used. For comparing palatal/lip measurements one-way ANOVA was used. For both comparisons a p value of less than 0.05 was considered to be significant. For statistical analysis of nasolabial aesthetics, a chi square test was done for all 11 questions comparing the number of favorable versus unfavorable outcomes. Fischer's exact test was used if the number of cases in a group was less than 5. Bonferroni correction was used to correct for multiple comparisons for the nasolabial aesthetics; a p of less than 0.005 was considered significant based on this correction. Cohen's kappa coefficient was used to calculate intra-rater

reliability for all categorical measurements. All statistical comparisons were calculated using IBM SPSS TM software.

1.4 RESULTS

1.4.1 Patient Demographics

A total of 104 patients were included in this study; 39 patients received treatment with an active device, 31 patients received treatment with a passive device, and 34 patients did not receive treatment with a PSO device. The active device was inserted at an average age of 2.2 months. Table 3 outlines the remaining demographic information for the study population. Age at cheiloplasty was significantly different between the three groups ($p<0.01$), but there was no statistical difference in the age that patients had palatoplasty ($p=0.89$). The rate of lip revision in the active, passive, and no device groups was as follows: 7.69% active, 32.3% passive, 14.7% no device ($p=0.03$). Otherwise, there was no statistical difference between the groups for the remaining demographic variables.

Table 4 outlines measurements for vertical AG, horizontal AG, palate width at posterior hard palate, cleft width at posterior hard palate, and alar base width of the cleft and non-cleft side for all 3 groups. For initial vertical and horizontal alveolar gap measurements there was a significant difference between the groups ($p<0.01$, $p<0.01$); patients with no device had smaller gaps than patients with an active ($p<0.01$, $p<0.01$) or a passive device ($p=0.01$, $p<0.01$). For initial cleft and non-cleft side alar base measurements there was a significant difference between the groups ($p<0.01$, $p<0.01$); patients with no device had smaller cleft-side and non-cleft side alar base measurements than patients with an active ($p<0.01$, $p=0.02$) or a passive device ($p<0.01$, $p=0.01$). At the time of lip repair non-cleft side alar base measurements were similar ($p=0.24$), but different on the cleft side ($p<0.01$). Vertical AG was similar between the 3 groups at lip repair ($p=0.11$) and palate repair ($p=0.54$). Horizontal AG was significantly different at lip repair ($p<0.01$) but not significantly different at the time of palate repair ($p=0.54$). Posterior cleft width and palate width were not statistically different between the three groups at palate repair ($p=0.15$, $p=0.29$). There was no significant difference between patients who

received or did not receive a lip revision surgery based on the size of their horizontal or vertical alveolar gap at the initial visit ($p=0.17$, $p=0.07$) or at lip repair ($p=0.38$, $p=0.57$).

1.4.2 Intra-rater Reliability

Intra-rater reliability measurements were calculated for all of the initial AG measurements. Intra-class correlation coefficient values were over 0.90 for all alveolar gap measurements which indicates excellent intra-rater reliability.

Active PSO n= 39	Passive PSO n= 31	No PSO n= 34	P value
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Basic Demographic Information	M:F	27:12	19:12	22:10	0.78
	L:R Sided Clefts	25:14	20:11	17:16	0.47
	Family History	16/31	7/24	6/18	0.20
	Smoking Mother	5/22	5/20	6/13	0.34
Cheiloplasty	Age	4.3 months	5.2 months	3.9 months	<u><0.01</u>
	Lip Adhesion	0 Lip adhesion	2 Lip adhesion	2 Lip adhesion	
Palatoplasty	Age	12.3 months	12.1 months	12.2 months	0.89
	Surgery	34 Hybrid	18 Hybrid	13 Hybrid	0.15
		3 Furlow	6 Furlow	4 Furlow	
		2 Unknown	7 Unknown	17 Unknown	
Lip Revision	Yes:No	1:38	9:22	5:21	<u>0.03</u>
	Reason for revision	1 Scar >3mm	2 Hyper. scar	1 Hyper. scar	
			5 Scar >3mm	4 Scar >3mm	
			1 Ala narrow		
			1 Unknown		

Table 3: Demographic information for study cohort. M=male, F= female, L= left, R=right, Hyper= hypertrophic

		Active PSO n= 39	Passive PSO n= 31	No PSO n= 24	P value
Initial (mm)	Vertical AG	9.44	7.43	3.93	<u><0.01</u>
	Horizontal AG	6.16	6.18	1.89	<u><0.01</u>
	Alar Base (Cleft)	15.8	14.1	11.1	<u><0.01</u>
	Alar Base (Non-Cleft)	6.10	7.66	5.02	<u><0.01</u>
Lip Repair (mm)	Vertical AG	5.08	7.23	3.93	0.11
	Horizontal AG	2.70	7.26	1.89	<u><0.01</u>
	Alar Base (Cleft)	16.1	13.0	11.1	<u><0.01</u>
	Alar Base (Non-Cleft)	4.98	5.40	5.02	0.24
Palate Repair (mm)	Vertical AG	2.26	2.90	1.73	0.54
	Horizontal AG	0.59	2.54	0.15	0.09
	Palate Width	29.1	29.9	30.8	0.29
	Posterior Cleft Width	11.7	9.57	6.13	0.15

Table 4: Alveolar gap measurements for patient cohort.

1.4.3 Nasolabial Aesthetics

The following patients had photographs for nasolabial aesthetic assessment at the 1-year mark: 31 active device, 30 passive device, and 31 patients with no device. At the 1-year mark there was no significant difference between the 3 groups for any of the 11 nasolabial outcomes measured (Figure 23). Age that the photographs were taken was also not significantly different between the 3 groups at the 1-year mark ($p=0.25$). At the 5-year mark the following patients had photographs for analysis: 30 active device, 23 passive device, and 26 patients with no device. There was no significant difference between the 3 groups for nasolabial aesthetics or age of the photographs at the 5-year mark (Figure 24). At the 10-year mark the following patients had photographs for analysis: 18 active device, 24 passive device, and 22 patients with no device. There was no significant difference between the groups for nasolabial aesthetics at the 10-year mark (Figure 25). There was a significant difference in the age that photographs were taken; patients with an active device had photos taken at an average of 8.59 years, patients with a passive device had photos at 9.77 years, and patients with no device had photos at 9.75 years ($p<0.01$). When all 11 variables were combined into an overall score, there was no significant difference between the 3 groups at the 1-year, 5-year, or 10-year mark (Figure 26, Table 5).

1.4.4 Sub-group Analysis

A separate analysis was also performed to control for the different rates of lip revision between the 3 groups. A repeat analysis was performed with all patients who received lip revision surgery excluded. There was no significant difference between the 3 groups for any nasolabial aesthetic measurements at the 1-year, 5-year, or 10-year mark.

1.4.5 Intra-rater Reliability

Intra-rater reliability was calculated using Cohen's kappa coefficient. Kappa coefficient was 0.791 which indicates substantial intra-rater reliability.

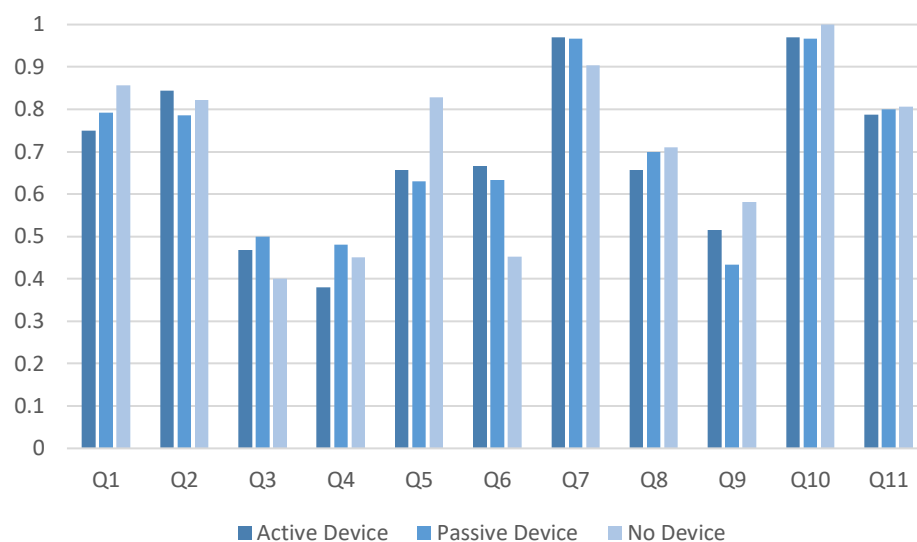


Figure 23: Percent favorable outcomes for each question of the nasolabial aesthetic scale at the 1-year mark.

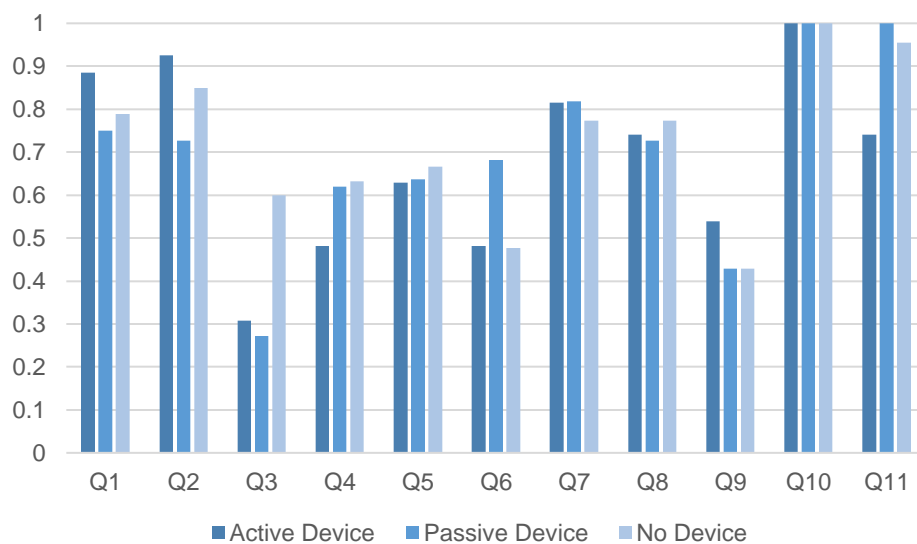


Figure 24: Percent favorable outcomes for each question of the nasolabial aesthetic scale at the 5-year mark.

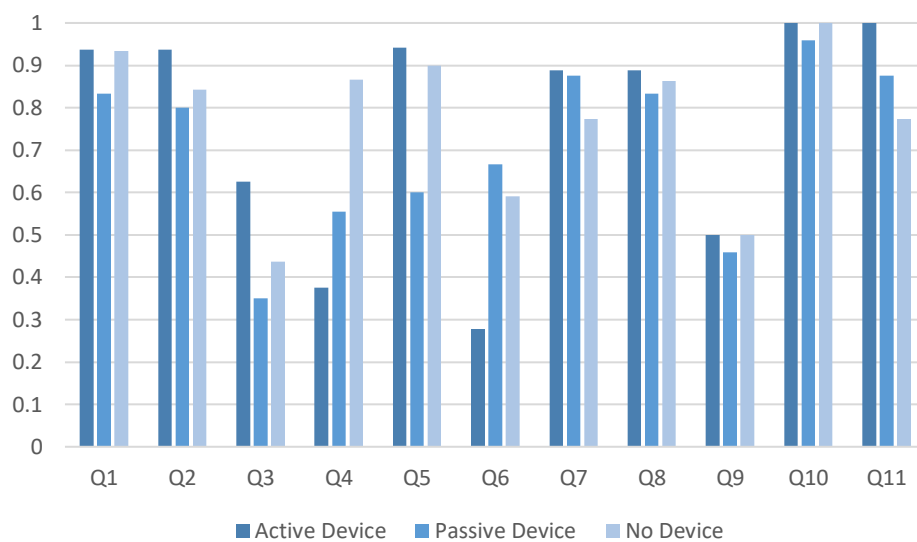


Figure 25: Percent favorable outcomes for each question of the nasolabial aesthetic scale at the 10-year mark.

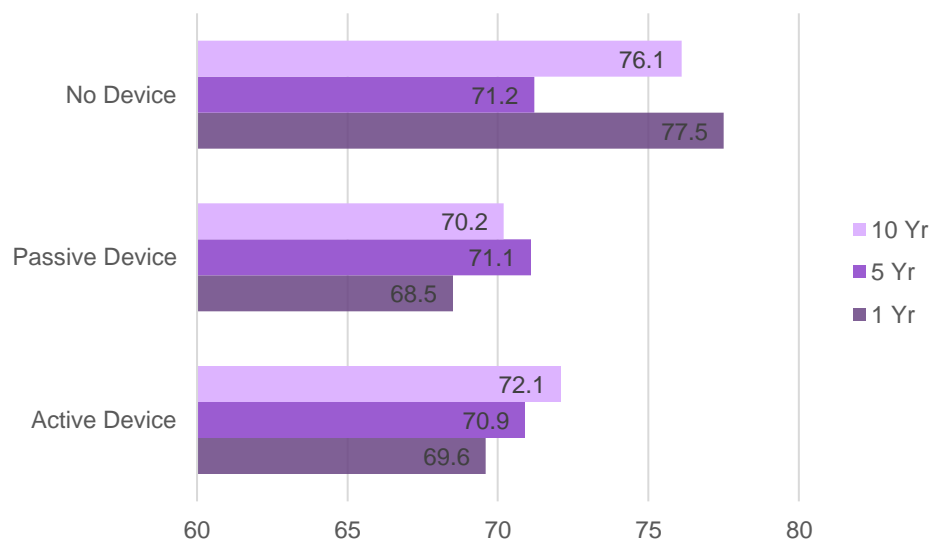


Figure 26: Percent Overall Favorable Nasolabial Outcomes.

		Active PSO n= 39	Passive PSO n= 31	No PSO n= 34	P Value	Subgroup Analysis
1-Year	N	31	30	31		
	Age (years)	1.34	1.08	1.14	0.08	0.25
	Overall Outcome	69.6%	70.9%	72.1%	0.80	0.39
5-Year	N	30	23	26		
	Age (years)	4.23	5.15	4.86	0.06	0.15
	Overall Outcome	68.5%	71.1%	70.2%	0.82	0.52
	Growth 1 to 5 Yr	+1.04%	+0.84%	+0.40%	1.00	
10-Year	N	18	24	22		
	Age (years)	8.59	9.77	9.75	<u><0.01</u>	0.03
	Overall Outcome	77.5%	71.2%	76.1%	0.21	0.62
	Growth 5 to 10 Yr	+5.58%	+1.86%	+4.78%	0.80	

Table 5: Percent favorable outcomes and growth between groups at 1, 5, and 10 years. Subgroup analysis excluded patients with lip revision surgery.

1.5 DISCUSSION

The long-term effects of PSO devices on nasolabial aesthetics are still highly debated. The current literature that exists is limited by patient groups that are operated on by different surgeons using different protocols. This variability limits the conclusions that can be drawn from this research. This study is the first single-surgeon study to examine the long-term effects of PSO devices on nasolabial aesthetics in patients whose management protocol only differed based on which PSO device was used.

In this study, nasolabial aesthetics were compared between patients treated with an active PSO device, a passive PSO device, and patients treated without a PSO device. All 3 patient groups had similar demographic factors. Patients that were treated with a passive device had lip repair surgery performed later than the other 2 groups. This is an expected finding; passive devices take longer to re-approximate the edges of the alveolar gap which does delay lip repair. All 3 groups had palate repair at the same time (range 12.1 to 12.3 months) and a similar distribution of types of palate repair. Patients treated with PSO devices had initially larger vertical and horizontal alveolar gaps as well as cleft and non-cleft side alar base measurements compared to patients without a device. This is also an expected finding; patients with more severe alveolar gaps are the ones that are offered a PSO device. Specifically, patients treated with a passive device had larger horizontal AG measurements at lip repair. This may be secondary to the fact that passive devices mold the alveolar elements and do not drive them together like the active device does. Secondly, patients treated with an active device had larger cleft-side alar base measurements at lip repair. This difference may be due to the lack of nasal molding associated with active devices; passive devices have a nasal molding component while active devices do not. Despite these initial differences between groups, by the time of palate repair there was no significant difference in the size of the AG in all 3 groups.

Patients with passive devices had higher rates of lip revision surgery compared to patients with active devices or no device. The majority of patients had a lip revision over concerns for scarring, specifically a hypertrophic or wide scar. The decision to undergo revision is usually a joint decision between the surgeon and the patient's family. There was no record of whether these patients underwent scar revision due to suggestion from the family or the surgeon. This makes it difficult to comment on whether patients and their families were dissatisfied with the scarring outcomes. One possible explanation for the higher rates of lip revision surgery in patients treated with a passive device may be that the larger horizontal AG at the time of lip repair made the repair more challenging. A tighter repair could have led to more tension on the closure and higher rates of dehiscence. Despite this possible explanation, a wider AG at lip repair was not associated with increased risk of lip revision surgery. Since scarring was not found to be significantly different between the 3 groups and increased AG width was not found to be associated with higher rates of scar revision, other factors that were not described in this study are likely the cause of the difference in the rate of scar revision between the groups.

Looking specifically at the nasolabial outcomes, all aspects of the nasolabial assessment were similar between the 3 groups at the 1-year, 5-year, and 10-year mark. Sub-group analysis eliminating all patients that received a lip revision surgery was also performed to ensure that lip revision was not a confounding factor. There was no change in the significance of the results which indicates that lip revision did not confound the nasolabial aesthetic findings. Overall, the similarity in nasolabial aesthetics between these 3 groups indicates that despite starting with different alveolar gap sizes, patients treated with PSO devices have comparable nasolabial aesthetic up to 10 years of age.

Looking specifically at the comparison between patients treated with active or passive PSO devices, it is important to recognize that there was no difference in nasal outcomes (e.g. columellar deviation, nasal recurvatum) between the 2 groups. Passive molding devices have previously been shown to improve nasal

outcomes including columellar deviation/height and alar base symmetry (35,139). These supposed nasal benefits are a motivating factor for the use of a passive device over an active device (140). However, the results of this study indicate that the passive device does not achieve superior nasal outcomes compared to the active device.

Overall, PSO devices were used in our patient population for patients with more severe AGs. Based on the results of this current study, active and passive PSO devices give patients with more severe AGs nasolabial aesthetic outcomes that are comparable to patients with less severe AGs. Furthermore, this study showed that passive molding does not provide superior nasal aesthetic outcomes compared to molding with an active device. Moving forward, a prospective study comparing these 3 groups matched for AG severity would determine whether PSO devices help achieve superior nasolabial aesthetics compared to patients with similar clefts treated without a device.

1.6 CONCLUSION

Overall, the objective of this study was to compare nasolabial aesthetics between patients treated with active or passive PSO devices to those treated without a PSO device up to 10 years of age. The results of this study show that patients treated with a PSO device start with larger AGs, but the PSO device is able to decrease the AG to a size that is similar to a less severe or incomplete cleft. In addition, treatment with PSO devices gives patients starting with more severe AGs nasolabial aesthetics that are comparable to patients with less severe AGs that do not require PSO treatment. Finally, this study found that passive PSO devices are not superior to active devices for nasal aesthetics despite having a nasal molding component. Moving forward, a prospective study that compares the use of passive and active PSO devices to patients with no device that are matched for cleft severity would elucidate whether PSO devices directly improve nasolabial aesthetics, or whether aesthetics are dependent on other factors.

Chapter 4: 10-Year Dental Occlusion and Facial Growth Comparison in Patients Treated with Different Pre-surgical Orthopedic Devices

Long-term outcomes in patients with cleft palate that are treated with different pre-surgical orthopedic devices are still highly debated. There is no consensus in the literature about the long-term effects of these devices on dental occlusion and facial growth, and there is very little literature comparing different types of these devices. The purpose of this chapter is to evaluate and compare 10-year dental occlusion and facial growth in patients treated with active or passive pre-surgical orthopedic devices.

A portion of this work was presented at the Canadian Society of Plastic Surgeons (CSPS) 2020 annual meeting.

1.1 INTRODUCTION

A controversial topic in cleft lip/palate (CL/P) management is the use of pre-surgical orthopedic (PSO) devices. Broadly, PSO devices can be classified as either active or passive devices. Passive devices bring the edges of the alveolar gap closer together through the use of custom palatal molds (with or without nasal stents), while active devices use pins and screws to reapproximate the edges of the gap through active movement (35). Pre-surgical orthopedic devices were initially designed to be used in conjunction with gingivoperiosteoplasty (GPP) to reduce the size of the alveolar gap and create a more anatomic dental arch (35). Previous research has shown that active PSO devices in conjunction with GPP lead to decreased maxillary growth (44). Many surgeons have moved away from using GPP in conjunction with an active PSO device, but the effect of the active PSO device alone is still debated (54,123). Unlike research on active devices, to date there do not appear to be any studies that have looked at facial growth in patients treated with a passive device and GPP. Furthermore, the studies that have looked at facial growth outcomes in patients treated with a passive device alone show that the device has no effect on growth (114,126).

Given these differences reported in the literature, an important comparison that should be made is between patients receiving different types of PSO devices. There is currently very minimal research comparing different types of PSO devices (35). There is no consensus as to the effects of either of these devices on dental occlusion and growth. In addition, there are very few research publications actually comparing these two types of devices. Both of these types of devices have negatives and positives to their use; active devices require an additional anesthetic for insertion of the device while passive devices take longer to mold the palate (35). This comparison is important for determining if one device is superior to the other for reducing negative effects on facial growth and dental occlusion and would help guide practice moving forward.

At our institution, the same surgeon and orthodontist have treated a cohort of patients with CL/P for over 15 years. Both active and passive molding devices are offered to patients and their families. This presents the unique opportunity to compare outcomes in patients whose management only differs in the PSO device that they received. The objective of this research chapter is to compare the effects of active PSO devices and passive PSO devices on dental occlusion and facial growth in a single-surgeon's cohort of patients with CL/P over a 10-year period.

1.2 METHODOLOGY

A retrospective review of all patients with cleft lip and palate in a single surgeon's practice from 2002-2018 was performed. This cohort of patients was under the management of a multidisciplinary cleft palate group that consisted of a single palate surgeon, a single orthodontist, and a single speech language pathologist. All patients with a unilateral complete cleft of their primary palate treated with an active or passive pre-surgical device were identified. Patients were excluded if they had no molds or cephalograms taken, were not treated with a PSO device, had a known syndrome, had bilateral cleft lip or palate, or were not operated on by the primary surgeon. Patients were divided into two groups based on whether they received pre-surgical care with an active PSO device or a passive PSO device. Basic patient demographic information and initial alveolar gap measurements were collected as described in **CHAPTER 0**. Additional demographic patient information that was recorded for this study included patients who received bone graft surgery, were diagnosed with velopharyngeal insufficiency (VPI), or had treatment with braces/elastics and protraction face masks. Patients were excluded from calculation of the rate of braces application and bone graft surgery if they were under the age of 8 as these patients are too young for such treatments.

1.2.1 Dental Occlusion

Patient molds are taken at each patient visit; these molds are plaster casts of the maxillary and mandibular dentition (Figure 9). All patient molds were evaluated and measured by a single blinded reviewer. A subset of 20 randomly selected molds were analysed a total of 3 separate times over the course of 1 month to calculate intra-rater reliability. Dental occlusion was assessed by putting molds in anatomic alignment and measuring occlusion based on the Angle classification (Figure 8), GOSLON Yardstick classification (Figure 9), Modified Huddart Bodenham (MHB) classification (Figure 10), and dental arch measurements (Figure 11).

The Angle classification was assessed using the bilateral molars; the second molar was used to calculate the Angle score for primary dentition and the first molar was used to calculate the Angle score for mixed/permanent dentition. For classifying Angle occlusion, half a cusp of anterior or posterior displacement was considered abnormal and qualified as Grade 2/3. If the Angle scores on the left and right side differed, the more severe occlusal grade was recorded for each mold.

The GOSLON Yardstick classification was assessed by measuring the overjet between the upper and lower central incisors with a boley gage to the nearest 1/10 of a millimeter. Occlusion was then graded based on the amount of overjet measured. Overall GOSLON yardstick grade and overjet (in millimeters) were recorded for each mold.

Overall grade for the MHB classification was calculated as the sum of each individual grade. If a maxillary tooth was missing for MHB analysis, the grade was assessed by using the position of the mandibular tooth compared to the midpoint of the maxillary arch. If the maxillary and the corresponding mandibular tooth were both missing, the average MHB grade of the two surrounding teeth was used.

Dental arch measurements were measured as described in **CHAPTER 0** using electronic calipers to the nearest 1/100 of a millimetre. Dental arch measurements included inter-canine width (ICW), inter-palatal molar width (IPMW), and the sum of the incisors (SI). If a maxillary tooth required for measurement was missing, the measurement was taken from the centre of the alveolar arch in line with the corresponding contralateral tooth.

1.2.2 Cephalometric Analysis

Patient radiographs are taken at 5 and 10 years during their follow-up visits. These radiographs were digitized and analysed using the Dolphin Imaging™

cephalometric software. Each cephalogram was standardized for magnification using a 40mm ruler included in each radiograph. Standard cephalometric landmarks were plotted by 2 reviewers who reached a consensus about the placement of each plotted landmark. Each radiograph was analyzed in a random order. A subset of 10 randomly selected radiographs were analysed on 3 separate occasions over the course of 1 month to calculate intra-rater reliability. Cephalometric measurements were derived from the plotted landmarks; the Dolphin Imaging™ program calculates cephalometric measurements based on these plotted landmarks. Table 1 describes each of the cephalometric measurements that were calculated by Dolphin Imaging™. Overall, maxillary, mandibular, vertical, dento-alveolar, and soft tissue landmarks were calculated.

1.2.3 Statistical Analysis

For statistical analysis, mean Angle score, GOSLON yardstick score, MHB score, and dental arch measurements were compared between the 2 groups using an independent sample t-test. Fischer's exact test was used to compare the distribution of patients with each Angle score and GOSLON yardstick score. Changes in occlusion and dental arch were also calculated for all patients that had 5 and 10-year measurements. This was calculated as the 10-year measurement minus the 5-year measurement. The means of these growth measurements were also compared via independent sample t-tests. Bonferroni correction was used to correct for multiple comparisons of occlusion.

For cephalometric measurements, measurements for patients with an active PSO versus a passive PSO were calculated using independent sample t-tests. Growth changes were also calculated for all patients that had 5-year and 10-year cephalometric measurements. Growth was calculated as the 10-year cephalometric measurement minus the 5-year cephalometric measurement. The means of these growth measurements were also compared via independent

sample t-tests. Bonferroni correction was used to correct for multiple comparisons of cephalometric measurements.

Intra-class correlation coefficient (ICC) was calculated for intra-rater reliability of all measured values. Cohen's kappa coefficient was used to calculate intra-rater reliability for all categorical measurements. All statistics were calculated using IBM SPSS TM software.

1.3 RESULTS

1.3.1 Demographic Information

Twenty patients with an active device and 23 patients with a passive device were included in this study. No differences were observed in the male/female distribution, left/right-sided cleft distribution, risk factors for cleft development, age and type of lip repair, age and type of palate repair, use of face masks, use of braces, rate of lip revision surgery, rate of bone grafting, and rate of VPI development between experimental groups (Table 6). Cleft measurements, alar base measurements, and palatal width measurements were statistically insignificant between the two groups at their initial visits. At the time of lip repair, patients with a passive device had significantly larger horizontal alveolar gaps but smaller cleft-sided alar base measurements ($p < 0.01$, $p < 0.01$). At the time of palate repair, the difference in anatomic measurements between the two groups was insignificant (Table 7).

		Active PSO n= 20	Passive PSO n= 22	P value
Basic Demographic Information	M:F	14:6	14:8	0.75
	L:R Sided Clefts	13:7	13:9	0.69
	Family History of Cleft	41.2%	33.3%	0.63
	Smoking Mother	33.3%	18.8%	0.66
Cheiloplasty	Age	4.5 months	5.1 months	0.29
	Surgery	20 Mohler	18 Mohler	0.49
		0 Millard	2 Millard	
		0 Unknown	1 Unknown	
	Lip Adhesion	0 Lip adhesion	1 Lip adhesion	
Palatoplasty	Age	12.3 months	12.0 months	0.59
	Surgery	19 Hybrid	12 Hybrid	0.08
		1 Furlow	5 Furlow	
		0 Unknown	5 Unknown	
Braces/Elastics	Yes:No:N/A	6:5:9	14:8	0.46
Face Masks	Yes:No	1:19	6:16	0.10
Lip Revision	Yes:No	2:18	7:15	0.07
Bone Graft	Yes:No:N/A	7:4:9	19:2:1	0.15
VPI	Yes:No:N/A	4:7:9	5:16:1	0.68

Table 6: Basic demographic information for experimental groups. VPI= velopharyngeal insufficiency. N/A indicates patient too young to assess.

		Active PSO	Passive PSO	P value
		n= 20	n= 22	
Initial Measurements (mm)	Vertical AG	9.37	7.25	0.16
	Horizontal AG	6.28	6.46	0.87
	Palate Width	29.8	28.9	0.48
	Posterior Cleft Width	15.6	16.2	0.66
	Alar Base (Cleft)	15.6	14.0	0.21
	Alar Base (NC)	6.22	8.04	0.05
Lip Repair Measurements (mm)	Vertical AG	5.10	8.19	0.06
	Horizontal AG	3.15	9.97	<u><0.01</u>
	Alar Base (Cleft)	16.5	11.9	<u><0.01</u>
	Alar Base (NC)	5.24	5.56	0.36
Palate Repair Measurements (mm)	Vertical AG	1.75	4.00	0.41
	Horizontal AG	0.66	1.00	0.94
	Palate Width	30.8	29.9	0.38
	Posterior Cleft Width	14.4	10.5	0.58

Table 7: Anatomic measurements for assessing cleft severity at initial visit, lip repair, and palate repair. NC= non-cleft side

1.3.2 Dental Arch and Occlusion

For the 5-year dental analysis, 20 patients with an active device and 20 patients with a passive device had molds for analysis. There was no significant difference in the average Angle classification, MHB classification, and GOSLON yardstick classifications between the three groups ($p=0.86$, $p=0.74$, $p=0.73$) (Table 8). Average Angle classification was: 2.15 for the active group and 2.20 for the passive group. All 3 patient groups showed no statistical difference in the number of patients with Angle class 1, 2, or 3 classification ($p=1.00$) (Figure 27). Average MHB classification was -7.50 for the active group and -6.85 for the passive group ($p=0.74$). Average GOSLON yardstick classification was: 3.20 for the active group and 3.15 for the passive group ($p=0.73$). Both patient groups showed no statistical difference in the number of patients with GOSLON yardstick class 1, 2, 3, 4, and 5 occlusion ($p=0.79$) (Figure 28). Average amount of central incisor overjet was -0.07mm for the active group and 0.12mm for the passive group ($p=0.82$). Average inter-canine and inter-palatal molar width for each group was: 25.7mm and 35.0mm for the active group, and 25.9mm and 33.8mm for the passive group ($p=0.81$, $p=0.45$). Average sum of incisor measurements was: 21.7mm and 21.9mm for the active and passive groups respectively ($p=0.79$) (Table 9). Average age of device measurement was 5.60 years in the active group and 6.24 in the passive group ($p=0.05$).

For the 10-year dental analysis 15 patients with an active device and 22 patients with a passive device had molds for analysis. There was no significant difference in the Angle classification, MHB classification, and GOSLON yardstick classifications between the two groups ($p=0.93$, $p=0.58$, $p=0.13$) (Table 8). Average Angle classification was: 2.07 for the active group and 2.05 for the passive group ($p=0.93$). Patients with an active PSO device and a passive PSO device had no statistical difference in the distribution of patients with Angle class 1, 2, and 3 classification ($p=0.35$) (Figure 29). Average MHB classification was -6.43 for the active group and -5.41 for the passive group ($p=0.58$). Average GOSLON yardstick

classification was: 3.00 for the active group and 2.59 for the passive group ($p=0.13$). There was no significant difference in the distribution of patients with GOSLON yardstick class 1, 2, 3, 4, and 5 occlusion ($p=0.14$) (Figure 30). Average amount of central incisor overjet was: 0.70mm in active patients and 0.40mm in passive patients ($p=0.73$). Average inter-canine and inter-palatal molar width for each group was: 28.5 mm and 42.7mm for the active group, and 29.8mm and 40.3mm for the passive group ($p=0.41$, $p=0.10$). Average sum of incisor measurements was: 24.0mm and 26.2mm for the active and passive groups respectively ($p=0.14$) (Table 9). Average age of device measurement was 9.37 years in the active group and 9.95 in the passive group ($p=0.18$).

1.3.3 Change in Dental Arch Relationships and Occlusion from Five to Ten Years

Fifteen patients from the active device group and 19 patients from the passive device group had 5-year and 10-year molds for evaluation of changes over the 5-year period (Figure 31). Average change in Angle classification from 5 to 10 years was -0.33 for active device patients and -0.26 for passive device patients ($p=0.87$). Change in MHB classification was 0.80 for active device patients and 2.11 for patients with a passive device ($p=0.57$). The change in GOSLON yardstick scoring for the groups was -0.27 for the active group and -0.79 for the passive device ($p=0.31$). Change in overjet was 0.85mm for active device patients and 0.48mm for passive device ($p=0.77$). Change in inter-canine width for patients was not significant ($p=0.12$). Change was 2.15mm for patients with an active device and 4.58mm for patients with a passive device. Change in inter-palatal molar width for active and passive device patients was 7.06mm and 6.72mm respectively ($p=0.82$). Finally, change in sum of incisors for active and passive device patients was 1.83mm and 4.70mm respectively ($p=0.07$).

1.3.4 Intra-rater Reliability

Intra-rater reliability was calculated using Cohen's kappa coefficient for Angle classification and GOSLON yardstick classification. The kappa value for intra-rater reliability of the Angle classification and GOSLON yardstick was 0.53 and 0.80 which represent moderate and substantial intra-rater reliability. Intra-class correlation coefficient was used to calculate intra-rater reliability for MHB classification, overjet, ICW, IPMW, and SI. The ICC was 0.88 for MHB which indicates good intra-rater reliability. The ICC was 0.86 for overjet measurements which indicates good intra-rater reliability. The ICC for ICW measurements was 0.67 which indicates good intra-rater reliability. The ICC for IPMW measurements was 0.80 which indicates good intra-rater reliability. The ICC for SI measurements was 0.85 which indicates good intra-rater reliability.

N for 5 years, 10 years		Active PSO n= 20, n= 15	Passive PSO n= 20, n= 22	P value
5 years	Mean age (years)	5.60	6.24	<u>0.05</u>
	Range	(4.92-8.83)	(4.92-8.33)	
	Standard Deviation	SD 0.92	SD 1.04	
	Angle Classification	2.15	2.20	0.86
	Standard Deviation	SD 0.94	SD 0.89	
	MHB Classification	-7.50	-6.85	0.74
	Range	(-17.0-3.00)	(-19.0-5.00)	
10 years	Standard Deviation	SD 6.53	SD 5.78	
	GOSLON Yardstick	3.20	3.15	0.73
	Standard Deviation	SD 1.37	SD 1.27	
	Mean age (years)	9.37	9.95	0.18
	Range	(7.00-12.3)	(7.67-11.4)	
	Standard Deviation	SD 1.62	SD 0.95	
	Angle Classification	2.07	2.05	0.93
	Standard Deviation	SD 0.71	SD 0.79	
	MHB Classification	-6.43	-5.41	0.58
	Range	(-22.0-9.00)	(-24.0-5.00)	
	Standard Deviation	SD 9.85	SD 7.99	
	GOSLON Yardstick	3.00	2.59	0.13
	Standard Deviation	SD 1.72	SD 1.22	

Table 8: Angle, MHB, and GOSLON Yardstick classification at 5 and 10 years.

N for 5 years, 10 years		Active PSO n= 20, n= 15	Passive PSO n= 20, n= 22	P value
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5 years	Overjet (mm) Range Standard Deviation	-0.07 (-6.50-4.10) SD 3.03	0.12 (-4.10-4.10) SD 2.21	0.82
	Inter-canine width (mm) Range Standard Deviation	25.7 (18.2-28.3) SD 2.36	25.9 (19.0-33.1) SD 3.92	0.81
	Inter-palatal molar width (mm) Range Standard Deviation	35.0 (28.2-44.0) 3.48	33.8 (24.1-48.4) 5.64	0.45
	Sum of incisors (mm) Range Standard Deviation	21.7 (18.6-28.7) SD 2.41	21.9 (15.1-27.0) SD 3.22	0.79
10 years	Overjet (mm) Range Standard Deviation	0.77 (-7.30-5.00) SD 3.87	0.40 (-5.00-5.00) SD 2.96	0.73
	Inter-canine width (mm) Range Standard Deviation	28.5 (20.9-36.8) SD 5.20	29.8 (19.7-39.0) SD 5.05	0.41
	Inter-palatal molar width (mm) Range Standard Deviation	42.7 (35.6-47.1) SD 3.77	40.3 (32.1-50.4) SD 3.79	0.10
	Sum of incisors (mm) Range Standard Deviation	24.0 (18.9-32.2) SD 4.43	26.2 (19.1-33.0) SD 3.88	0.14

Table 9: Overjet, inter-canine width, inter-palatal molar width, and sum of incisors at 5 and 10 years.

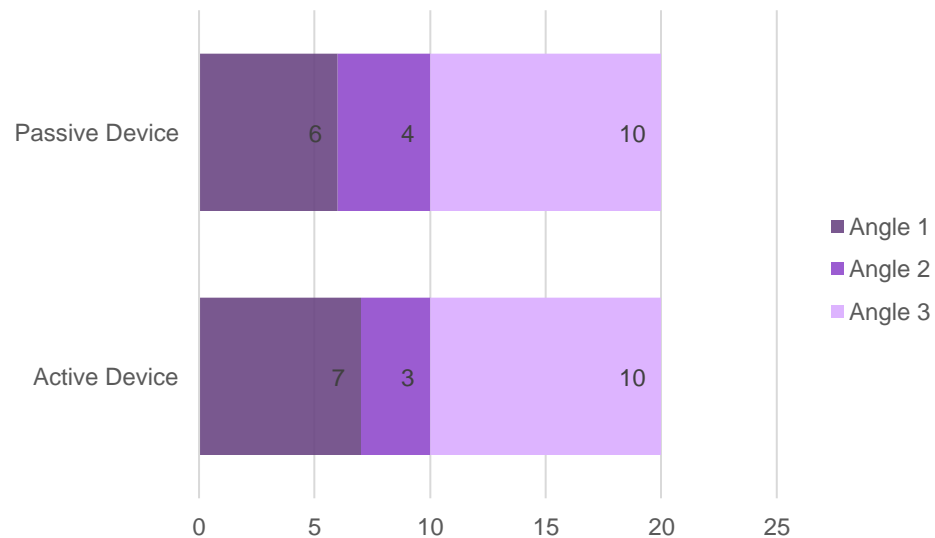


Figure 27: Number of patients in each Angle classification group at 5 years.

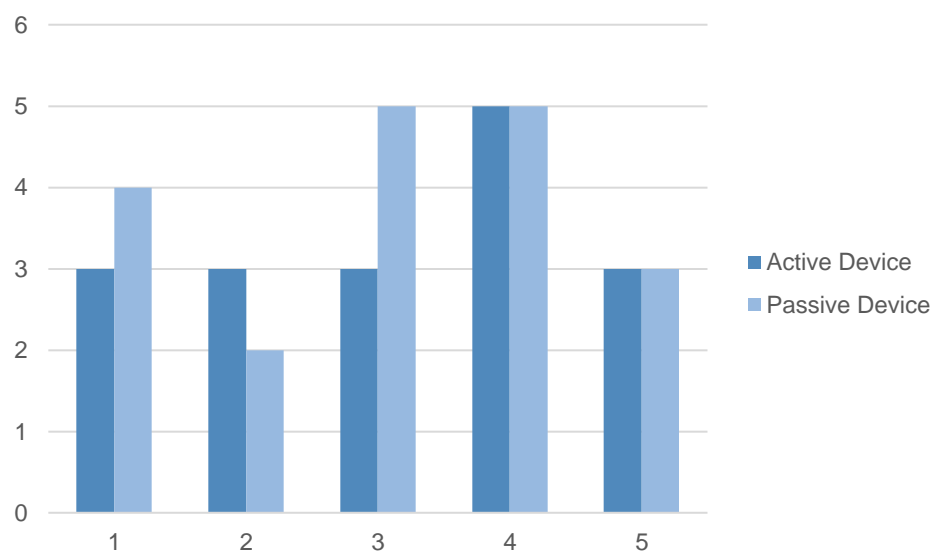


Figure 28: Number of patients in each GOSLON yardstick classification group at 5 years.

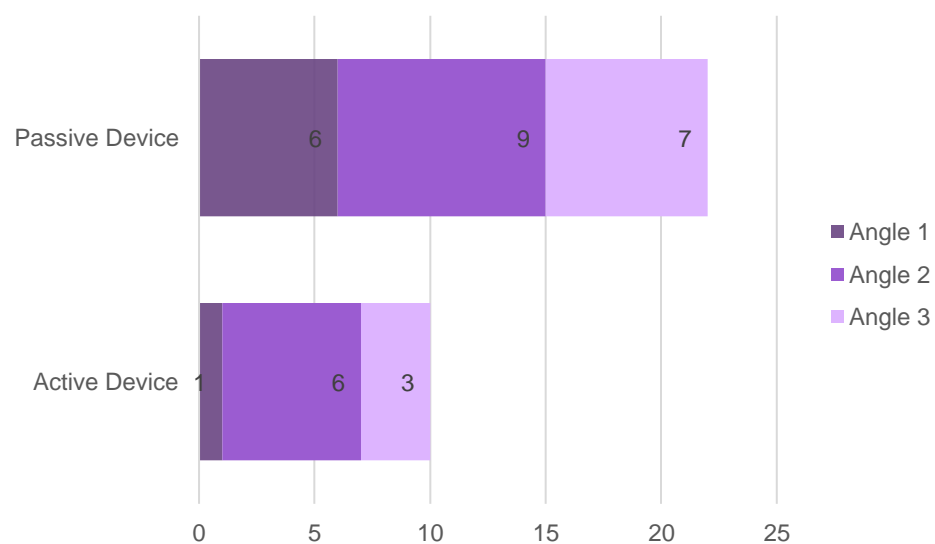


Figure 29: Number of patients in each Angle classification group at 10 years.

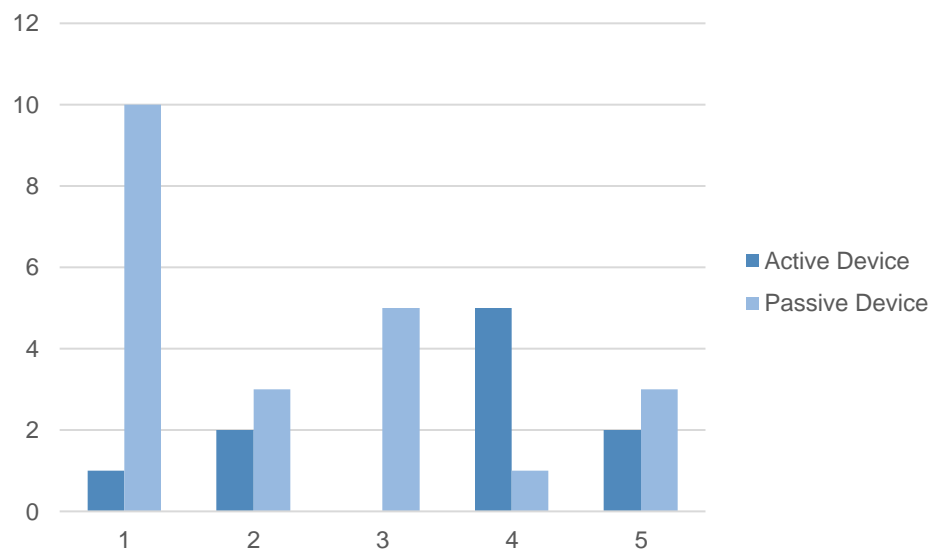


Figure 30: Number of patients in each GOSLON yardstick classification group at 10 years.

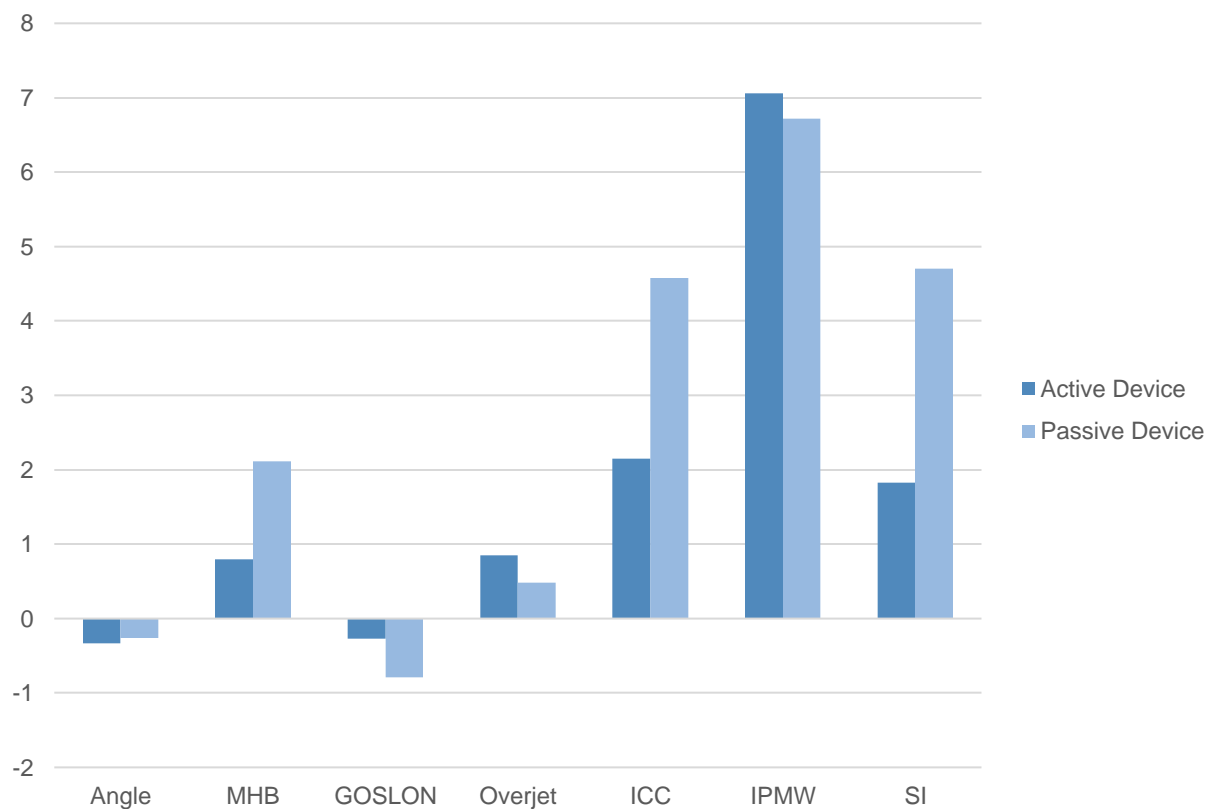


Figure 31: Change in occlusion and dental arch relationships from 5 to 10 years.

1.3.5 Cephalometric Measurements

For 5-year cephalometric analysis, mean age of measurements was 5.93 years (n=18) for patients in the active device group and 6.47 years (n=20) for patients in the passive group (p=0.17). For 10-year cephalometric analysis, mean age of measurements was 9.62 years (n=16) for patients with an active device and 9.97 years (n=23) for patients with a passive device (p=0.37).

1.3.6 Maxillary Growth Measurements

At 5 years, there was no significant difference between the two groups for the length of the maxillary palate (PNS-ANS), depth of the midface (Ba-A), length of the maxilla (Ba-ANS), maxillary protrusion (SNA), horizontal distance between nasion and A-point (N-A), maxillary position at A-point (Ba-N-A) and the maxillary position at ANS (Ba-N-ANS) (p=0.03, p=0.03, p=0.04, p=0.48, p=0.43, p=0.31, p=0.39). At 10 years, there was also no difference between the active and passive device patients (Table 10). A p-value of less than 0.01 was considered significant using the Bonferroni correction.

N for 5 years, 10 years		Active PSO n= 18, n= 16	Passive PSO n= 20, n= 23	P value (<0.01)
5 years	Mean age (years)	5.93	6.47	0.17
	SNA (°)	77.7	78.8	0.48
	N-A (mm)	-3.99	-3.01	0.43
	PNS-ANS (mm)	41.8	45.1	0.03
	Ba-A (mm)	77.2	82.4	0.03
	Ba-ANS (mm)	80.7	85.9	0.04
	Ba-N-ANS (°)	63.1	64.6	0.39
	Ba-N-A (°)	58.5	60.0	0.31
10 years	Mean age (years)	9.62	9.97	0.37
	SNA (°)	75.0	76.1	0.44
	N-A (mm)	-7.10	-6.10	0.44
	PNS-ANS (mm)	44.6	43.3	0.51
	Ba-A (mm)	79.7	77.0	0.40
	Ba-ANS (mm)	83.9	80.9	0.37
	Ba-N-ANS (°)	61.5	61.5	1.00
	Ba-N-A (°)	56.6	56.8	0.83

Table 10: Maxillary growth measurements at 5 and 10 years. With Bonferroni correction p-value <0.01 was considered significant.

1.3.7 Mandibular Growth Measurements

Mandibular growth measurements were similar between both groups at the 5 and 10-year mark (Table 11). Mandibular growth measurements included mandibular protrusion (SNB), horizontal distance between nasion and B-point (N-B), horizontal distance between nasion and pogonion (N-Pg), mandibular position at the pogonion (Ba-N-Pg), and mandibular position at B-point (Ba-N-B). A p-value of less than 0.01 was considered significant using the Bonferroni correction.

N for 5 years, 10 years		Active PSO n= 18, n= 16	Passive PSO n= 20, n= 23	P value (<0.01)
5 years	Mean age (years)	5.93	6.47	0.17
	SNB (°)	74.0	75.1	0.42
	N-B	-11.9	-10.3	0.40
	N-Pg	-13.0	-11.1	0.36
	Ba-N-Pg (°)	55.1	56.6	0.14
	Ba-N-B (°)	54.8	56.3	0.18
10 years	Mean age (years)	9.62	9.97	0.37
	SNB (°)	74.1	74.5	0.74
	N-B	-13.2	-12.4	0.72
	N-Pg	-13.8	-12.5	0.60
	Ba-N-Pg (°)	56.4	56.2	0.88
	Ba-N-B (°)	55.6	55.3	0.83

Table 11: Mandibular growth at 5 and 10 years. With Bonferroni correction p-value <0.01 was considered significant.

1.3.8 Dento-alveolar Relationships

Dento-alveolar measurements were similar between groups at 5 and 10 years. Dentoalveolar measurements included position of maxilla relative to mandible (ANB), alveolus to basal bone measurement (ANS-N-A), and basal bone difference (ANS-N-Pg). There were no differences between the two groups at 5 and 10 years (Table 12). A p-value of less than 0.02 was considered significant using the Bonferroni correction.

N for 5 years, 10 years		Active PSO n= 18, n= 16	Passive PSO n= 20, n= 23	P value (<0.02)
5 years	Mean age (years)	5.93	6.47	0.84
	ANB (°)	3.68	3.69	1.00
	ANS-N-A (°)	4.66	4.59	0.91
	ANS-N-Pg (°)	165.3	165.5	0.93
10 years	Mean age (years)	9.62	9.97	0.37
	ANB (°)	0.99	1.58	0.57
	ANS-N-A (°)	4.98	4.66	0.50
	ANS-N-Pg (°)	147.9	154.4	0.80

Table 12: Dento-alveolar growth measurements at 5 and 10 years. With Bonferroni correction p-value <0.02 was considered significant.

1.3.9 Vertical Facial Growth

At 5 and 10 years there was no significant difference between the groups for any vertical facial growth factors (Table 13). Vertical facial growth factors included upper facial height (N-ANS), lower facial height (ANS-Me), upper to lower facial height ratio (N-ANS/ANS-Me), and midface percent of total facial height (N-ANS/N-Me) were not significantly different between the two groups. A p-value of less than 0.01 was considered significant using the Bonferroni correction.

N for 5 years, 10 years		Active PSO n= 18, n= 13	Passive PSO n= 20, n= 23	P value (<0.01)
5 years	Mean age (years)	5.93	6.47	0.17
	N-ANS (ratio)	39.0	43.0	0.01
	ANS-Me (ratio)	58.2	56.9	0.03
	N-ANS/ANS-Me (ratio)	0.74	0.76	0.35
	N-ANS/N-Me (ratio)	0.43	0.44	0.42
10 years	Mean age (years)	9.62	9.97	0.37
	N-ANS (ratio)	44.3	44.3	0.98
	ANS-Me (ratio)	57.4	56.3	0.65
	N-ANS/ANS-Me (ratio)	0.77	0.79	0.46
	N-ANS/N-Me (ratio)	0.44	0.44	0.49

Table 13: Vertical facial growth measurements at 5 and 10 years. With Bonferroni correction p-value <0.01 was considered significant.

1.3.10 Soft Tissue Growth

Soft tissue growth measurements included soft tissue convexity, soft tissue profile, facial contour angle, and nasolabial angle (Table 14). There was no significant difference between groups at 5 and 10 years. A p-value of less than 0.02 was considered significant using the Bonferroni correction.

N for 5 years, 10 years		Active PSO n= 18, n= 13	Passive PSO n= 20, n= 23	P value (<0.02)
5 years	Mean age (years)	5.93	6.47	0.17
	Soft tissue convexity (°)	141.9	140.0	0.34
	Facial contour angle (°)	-5.54	-6.36	0.63
	Nasolabial angle (°)	110.7	113.1	0.45
10 years	Mean age (years)	9.62	9.97	0.37
	Soft tissue convexity (°)	143.7	140.8	0.12
	Facial contour angle (°)	-1.41	-5.11	0.06
	Nasolabial angle (°)	99.8	106.8	0.02

Table 14: Soft tissue growth at 5 and 10 years. With Bonferroni correction p-value <0.02 was considered significant.

1.3.11 Growth Between Five and Ten Years

A comparison of growth between the 5-year and 10-year measurements was also performed (Table 15). A total of 16 patients in the active device group and 18 patients in the passive device group had records for this comparison. Growth in the maxilla, mandible, dento-alveolar relationships, vertical facial height, and soft tissue values was not significantly different between the 2 groups.

1.3.12 Intra-rater Reliability

Intra-class correlation coefficient was calculated for cephalometric measurements. The ICC value was 0.81 which represents good intra-rater reliability.

N for 5 years, 10 years		Active PSO n= 16	Passive PSO n= 18	P value
Maxilla	SNA	-2.64	-2.93	0.80
	N-A	-3.08	-3.23	0.89
	PNS-ANS	2.53	-2.58	0.06
	Ba-A	2.01	-7.06	0.02
	Ba-ANS	2.63	-6.69	0.03
	Ba-N-ANS	-1.51	-3.41	0.21
	Ba-N-A	-1.81	-3.43	0.26
Mandible	SNB	0.33	-0.36	0.40
	N-B	-0.89	-1.45	0.64
	Pg-N	-0.28	-0.63	0.82
	Ba-N-Pg	1.74	-0.21	0.04
	Ba-N-B	1.17	-0.83	0.04
Dento-alveolar	ANB	-2.96	-2.61	0.70
	A-N-ANS	0.31	0.04	0.73
	N-ANS-Pg	-16.8	-14.5	0.94
Vertical Face	N-ANS	5.14	0.77	0.08
	ANS-Me	3.88	-2.47	0.03
	N-ANS/ANS-Me	0.04	0.45	0.79
	N-ANS/N-Me	0.01	0.11	0.78
Soft Tissue	Soft tissue convexity	1.39	0.70	0.70
	Facial contour angle	4.49	1.32	0.02
	Nasolabial angle	-11.7	-6.93	0.18

Table 15: Facial growth between 5 and 10 years. Significant p-values were considered <0.01 for maxilla growth, mandible growth, and vertical facial growth and <0.02 for dento-alveolar growth and soft tissue growth.

1.4 DISCUSSION

In the present study, patients being treated with a passive PSO device had significantly larger horizontal alveolar gaps at the time of lip repair. This discrepancy indicates that the passive device is not as effective at narrowing the alveolar gap compared to the active device. The patients treated with an active PSO device had larger cleft-side alar base measurements compared to the passive device patients at the time of lip repair. This could be explained by the fact that the passive device employs a nasal stent which also serves to mold the alar base, while patients with an active device had an intra-oral device that provides no nasal molding. By the time of palate repair patients in both device groups had similar measurements for alar base, palate width, and alveolar gap width. Patients in the active and passive device groups had similar rates of face mask application, braces application, lip revision, bone grafting, and VPI, all of which suggests that the patient group did not influence the number of additional procedures required following palate repair. In summary, patients in the active and passive device groups had comparable severity of their alveolar gap by the time of palate repair and similar management protocols. This is the first study comparing dental occlusion and facial growth where patients were matched for cleft severity and management protocol.

1.4.1 Dental Arch and Occlusion

The present study is the largest long-term study comparing dental arch relationships in patients treated with an active versus a passive PSO device. Overall, this study showed no difference in dental arch relationships between patients treated with an active or a passive device. All groups had an Angle classification grade that indicated a degree of overjet/overbite, a negative MHB score indicative of a degree of maxillary arch growth restriction (141), and a GOSLON yardstick score that indicates positive/minimal overjet and predicts good

outcomes following orthognathic surgery. When comparing changes from 5 to 10 years within patients, there were no differences between the groups. Angle classification, MHB score, GOSLON score, and overjet improved in both patient groups from 5 to 10 years although the changes did not reach significance. Improved occlusal scores from 5 to 10 years could be secondary to the use of braces and targeted dental extraction to allow for teeth to fit in anatomic alignment.

Assessing the width of the dental arch is important for determining whether patients have deficient palatal growth/expansion. While it has been shown that palatal surgery does cause some dental arch restriction, the effect of PSO devices on dental arch growth is unknown (142). To our knowledge, this is the first study to make the comparison in patients treated with active versus passive devices. When comparing the development of the dental arch in patients treated with a PSO device, there have been a handful of studies that have shown decreased maxillary arch collapse in patients treated with a passive device compared to no device (54,123,124). Unfortunately, these studies showing improved arch collapse only examined patients up to 18 months of age and so they cannot be used to extrapolate how the arch behaves as the patient grows older. A previous study by Banker et al. has reported that an IPMW to ICW ratio of 1:1 +/- 0.5 is indicative of normal arch development and a ratio of greater than 1.15:1 indicates deficient arch development (143). This ratio was 1.50 in patients with an active device and 1.35 in patients with a palate device, which indicates both patient groups had a degree of dental arch deficiency. This same study by Banker et al. also used an IPMW of under 34.92mm as an indicator for arch restriction. Using this criterion our patients would not be considered to have a restricted arch; at 10 years patients with an active device had an IPMW of 42.7mm and patients with a passive device had an IPMW of 40.3mm. Furthermore, both groups showed an overall expansion of the IPMW and the ICW from 5 to 10 years which is consistent with no restriction of the maxillary dental arch.

In summary, patients treated with an active device had comparable dental occlusion and dental arch width compared to patients treated with a passive device. The reported dental arch measurements indicate that there may be a small degree of maxillary arch restriction in both groups, although both groups still had growth in the arch from 5 to 10 years.

1.4.2 Facial Growth

Overall, this study found comparable facial growth outcomes between patients treated with an active versus a passive PSO device at 5 and 10 years. Before Bonferroni correction anterior/posterior and vertical maxillary growth was significantly smaller in patients treated with an active device at 5 years. Loss of significance following Bonferroni correction indicates that these differences can be explained by chance from repeated measurements and not by the effects of the device itself. The similarity in dentoalveolar relationships measured via cephalometric analysis reinforces the validity of the similar occlusal relationships that were found using the patient molds. Regarding the changes in growth from 5 to 10 years, patients had similar growth of the maxilla, mandible, dento-alveolar relationships, vertical facial height, and soft tissue values.

Previous research has shown that PSO devices, specifically active devices, cause a maxillary growth restriction (35,44). To our knowledge, there are few studies that have reported negative maxillary growth outcomes with the use of a passive device. The results from this study indicate that active devices do not restrict maxillary growth compared to passive devices. Furthermore, the reported average measurements for SNA angle (maxillary length) and SNB angle (mandibular length) in this study are similar to previously reported outcomes for patients with CL/P treated without a PSO device. Those studies reported an average SNA angle of 76.4 to 80.5 compared to our reported 75.0 to 78.9 and an SNB of 74.4 to 75.4 compared to our reported 74.0 to 75.1(144,145). While these groups cannot be

compared statistically because they are from different studies, this finding further supports our conclusion that the active and passive devices do not appear to negatively affect maxillary growth.

In summary, patients treated with an active device have similar facial growth to patients treated with a passive device up 10 years of age.

1.5 CONCLUSION

Overall, the results of this study indicate that dental occlusion/dental arch development and facial growth are similar between patients treated with an active or a passive PSO device. Patients treated with either device have a degree of overbite/overjet at the level of the molars (Angle 2) with good expected outcomes following orthognathic surgery (GOSLON 3). Neither device causes a significant amount of dental arch restriction. Overall, at 10 years patients in the active and passive device groups also have comparable facial growth. Moving forward, a prospective study that compares the use of passive and active PSO devices to patients with no device (with matched cleft severity) would elucidate whether patients with these devices develop occlusion and facial growth different to patients treated without a PSO device.

Chapter 5: General Discussion and Conclusion

This chapter will briefly outline the hypothesis and objectives of this thesis. This chapter will summarize the results of Chapter 2 through 4 and discuss weaknesses and strengths of each study. Finally, future directions of this study will be discussed.

1.1 SUMMARY

The purpose of this work was to review the current literature pertaining to long-term outcomes associated with pre-surgical orthopedic (PSO) devices used in the management of cleft lip and palate and to study the long-term effects of these devices.

The objectives of this thesis were to:

1. Perform a systematic review of current literature describing the long-term effects of different PSO devices used in the management of cleft palate. **(CHAPTER 0)**
2. To evaluate and compare 1-year, 5-year, and 10-year nasolabial aesthetic changes in patients who received treatment with an active PSO device, passive PSO device, or no PSO device. **(CHAPTER 0)**
3. To evaluate and compare 5-year and 10-year dental occlusion/dental arch development in patients who had treatment with an active PSO or passive PSO device. **(CHAPTER 0)**
4. To evaluate and compare 5-year and 10-year facial growth in patients who had treatment with an active PSO device or passive PSO device at 5 years and 10 years in order to determine whether there is a difference in facial development between these groups. **(CHAPTER 0)**

The findings of Chapters 2, 3, and 4 are reviewed below.

1.2 SUMMARY OF CHAPTER 2: SYSTEMATIC REVIEW OF THE LITERATURE ON THE LONG-TERM PATIENT OUTCOMES ASSOCIATED WITH PRE-SURGICAL ORTHOPEDIC DEVICES

The primary objective of this chapter was to perform a systematic review of the literature pertaining to long-term outcomes in patients who were treated with PSO devices. The search criteria were developed with assistance from a librarian and the results of the search were reviewed by 2 independent reviewers using strict inclusion and exclusion criteria. The reference lists of the included studies were also screened for inclusion.

The literature review produced a total of 41 articles for inclusion. These studies highlighted the existence of multiple confounding factors that often occur between comparison groups. These factors make it difficult to determine whether the reported outcomes are due to the devices or the confounding factors, and ultimately limit the applicability of the study results. Described confounding factors include the severity of the initial alveolar gap, different operating surgeons, and different management protocols. Secondly, the review highlighted that there is no consensus in the literature as to the long-term effects of PSO devices on patient outcomes. Thirdly, this systematic review highlighted the lack of studies comparing long-term patient outcomes between patients that are treated with active versus passive PSO devices. In summary, the results from this systematic review confirmed the initial study hypothesis that there is no consensus in the literature regarding the effects of these devices and that the literature that does exist is weakened by the heterogeneity that exists in between and within the different comparison groups.

1.3 SUMMARY OF CHAPTER 3: 10-YEAR NASOLABIAL AESTHETIC COMPARISON IN PATIENTS WITH DIFFERENT PRE-SURGICAL ORTHOPEDIC DEVICES

The primary objective of this chapter was to assess the 10-year nasolabial aesthetic outcomes of patients treated with an active PSO device, passive PSO device, or no device. Patients were included if they had a unilateral complete or incomplete primary cleft palate and were operated on by the principle surgeon. Nasolabial aesthetics were assessed using 2-dimensional facial photographs for patients taken at 3 time points (1 year, 5 years, 10 years). A total of 11 nasolabial variables were assessed for each photograph.

There were two principle findings in this study. The first finding was that patients treated with PSO devices had larger alveolar gaps compared to patients treated without a PSO device. Despite having worse alveolar gaps, patients treated with either PSO device had comparable 10-year nasolabial aesthetic outcomes to patients with less severe gaps that did not require device treatment. The second finding of this study was that despite passive devices providing a nasal molding component, there was no difference in nasal outcomes between patients treated with an active or a passive PSO device. Overall, PSO device treatment helps patients with more severe alveolar gaps achieve nasolabial aesthetic results similar to patients with less severe gaps.

1.4 SUMMARY OF CHAPTER 4: 10-YEAR DENTAL OCCLUSION AND FACIAL GROWTH COMPARISON IN PATIENTS WITH DIFFERENT PRE-SURGICAL ORTHOPEDIC DEVICES

The primary objective of this chapter was to compare the 10-year dental occlusion and facial growth outcomes in patients treated with an active PSO device versus a passive PSO device over a 10-year period. Dental occlusion was assessed by evaluating patients' dental models at 5 and 10 years. Facial growth was assessed through cephalometric analysis of lateral patient radiographs at the same time points.

There were 3 principle results found in this study. Firstly, patients treated with active or passive PSO devices had similar dental occlusion and dental arch development over a 10-year period. Secondly, neither PSO device cause a restriction in the growth of the maxillary arch. Thirdly, patients treated with an active PSO device had similar facial growth to patients treated with a passive device.

1.5 STRENGTHS AND LIMITATIONS

There are multiple strengths and weaknesses associated with this work. The strength of Chapter 2 lies in the fact that it provides a thorough summary of the current state of knowledge in this field. This systematic review was an exhaustive search of all literature pertaining to this subject. A meta-analysis would be a more powerful summary of results, but unfortunately the described results were too heterogenous for this type of analysis.

Chapters 3 and 4 share some similar strengths and weaknesses. In terms of weaknesses, both studies are retrospective. Retrospective studies may be influenced by selection bias. Strengths of these studies include that all groups were operated on by the same surgeon and had the same management protocol. These similarities help eliminate many confounding factors that could influence study results. Thirdly, these are 2 of the largest studies comparing these 3 groups over a 10-year period which makes this a very valuable study for understanding long-term patient outcomes. Finally, the 10-year follow-up period is another strength of the aforementioned studies. Frequently, cleft palate research is limited to follow-up at 1 to 5 years. A significant proportion of growth and development occurs between 5 and 10 years of age; an important factor to acknowledge when studying these populations. The 10-year follow-up period in this work accounts for important facial changes that can influence patient outcomes. Conversely, the follow-up period is also a weakness; patients still grow up to 18 to 20 years so growth changes following the 10-year follow-up period are not addressed.

Specific to Chapter 3, a limitation of this study was that patients in the PSO and no PSO device groups were not matched for alveolar gap severity; patients treated with no device had small complete or incomplete alveolar gaps and were often not treated with palate surgery. Palate surgery is a variable that is known to affect maxillary growth, which by extension could affect nasolabial aesthetics by changing lip protrusion. Patients in the no device group also had significantly less

severe alveolar gaps compared to patients treated with PSO devices. These differences are potential confounding factors and therefore, the patients treated with PSO devices versus no device cannot be directly compared in order to determine if using a PSO device is superior to not using a device. Despite this, it is still possible to judge whether the PSO devices make nasolabial aesthetics similar to nasolabial aesthetics in patients treated without a device who start with more severe alveolar gaps. Secondly, patients did differ in their rates of lip revision, but this was accounted for through analysis of patients excluding those who received lip revision surgery.

Specific to Chapter 4, the main limitation is also that it is a retrospective study. Therefore, some selection bias may exist between the two groups. A strength of this study was that the 2 comparison groups in this chapter were matched for alveolar gap severity. Very few studies in cleft palate research have groups matched for alveolar gap severity, which is a factor that could confound results. Secondly, to our knowledge this is the largest study comparing outcomes between patients treated with an active or passive PSO device with all possible surgical confounding factors eliminated.

1.6 FUTURE DIRECTIONS

Chapter 2 highlighted the necessity for a single-surgeon study examining the long-term nasolabial aesthetic, dental occlusion, and facial growth outcomes in patients treated with both active and passive PSO devices. In addition, this chapter also highlighted the need for studies actually comparing the different types of PSO devices. This is exactly what was performed in Chapters 3 and 4. In regard to future directions for this study, this study will be repeated in the next 3 to 4 years to examine 15-year outcomes in these patient groups. There are few 15-year follow-up studies in cleft palate literature, and currently no studies comparing active and passive PSO device patients who are matched for cleft severity. Unfortunately, the majority of the study patients are too young for 15-year follow-up analysis at this time, but this will be repeated when all of these study patients have reached 15 years old.

A question that this work does not answer is whether PSO devices are truly required to have adequate growth and aesthetic outcomes. To answer this question, patients treated with no device with alveolar gaps of equal severity would also need to be compared. A population like this does not currently exist in our patient cohort. A second future direction for this research could be a prospective study that directly compares nasolabial aesthetics, dental occlusion, and facial growth in patients treated with an active, passive, or no PSO device. A prospective study of this nature with groups that are matched for the severity of their alveolar gap would be an important way of assessing whether PSO devices are truly required to have improved facial growth and dental occlusion.

1.7 SIGNIFICANCE

The use of PSO devices for patients with cleft palate is still a highly debated topic. Surgeons base their decision to use a certain PSO device on experience, surgeon preference, and family preference. A lot of limitations exist in research on this subject, and Chapter 2 highlights a number of the limitations that exist in this area of research. This is the first systematic review to highlight these limitations in a quantitative manner. The significance of this systematic review is that it has highlighted the need for research with more strict methodology. This systematic review can be used to guide future research in this field.

Chapters 3 and 4 outlined the long-term effects of using passive and active PSO devices in patients with cleft lip/palate. These two studies are the first single-surgeon studies to examine the impact of both active and passive devices on nasolabial aesthetics, dental occlusion, and facial growth. In addition, these are the first single-surgeon studies to control for cleft severity and surgical management between the different patient groups. Overall, this is the largest study examining the long-term effects of PSO devices between patients treated with an active or a passive device where confounding factors including the operating surgeon, surgical management, and cleft severity are all controlled.

There is concern in the cleft palate community about how PSO devices affect maxillary growth, dental occlusion, and nasolabial aesthetics. Specifically, a large amount of concern lies in whether active devices reduce maxillary growth. The results from Chapter 4 allow us to conclude that overall, patients treated with an active device have comparable growth to patients treated with a passive device. These results may encourage surgeons who were hesitant to use active devices for this reason. Secondly, passive devices are often used in patients with cleft lip/palate for the nasal molding component. This work showed that passive devices do not produce superior nasal aesthetics compared to active PSO devices. Thirdly, this work showed that using a PSO device in larger clefts can help achieve

nasolabial aesthetic outcomes similar to patients with less severe clefts. Overall, the results of this work have disproven several current theories about PSO devices. This work can help guide cleft surgeons with their PSO device selection and may encourage the use of different PSO devices for different patients.

Appendices

1.8 APPENDIX 1- GLOSSARY

NAM device: passive PSO device

Latham device: active PSO device

Sella turcica (S): center of the sella turcica

Nasion (N): most superior point of the frontonasal suture

A point (A): most posterior point on the curve between the ANS and the PR

Anterior nasal spine (ANS): most anterior point on the maxilla at the level of the palate

Posterior nasal spine (PNS): most posterior point on the bony hard palate

Basion (Ba): most inferior posterior point on anterior rim of foramen magnum (tip of posterior cranial base)

B point (B): most posterior point of bony curvature of the mandible

Pogonion (Pg): most anterior point on mandibular symphysis

Menton (Me): lowest point on chin

Soft tissue nasion (N'): soft tissue marker of most superior point of the frontonasal suture

Soft tissue A-point (A'): soft tissue marker of most posterior point on the curve between the ANS and the PR

Soft tissue pogonion (Pg'): most anterior point on chin

Soft tissue gnathion (G'): most anterior inferior point

Pronasale (Pn): most anterior tip of nose

Columella (Col): midpoint on the lower surface of the nose

Subnasale (Sn): junction of where the base of the columella meets the upper lip

1.9 APPENDIX 2- NASOLABIAL AESTHETIC RATING SCALE

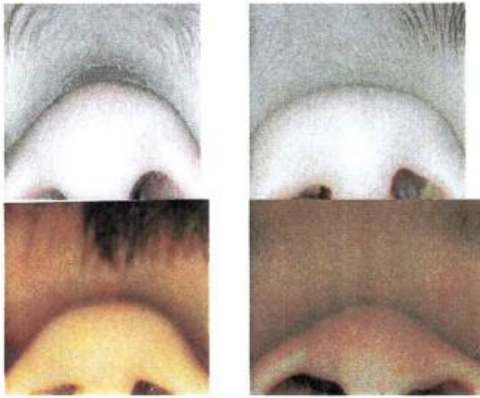
Q1: **Tip Symmetry** (use Folders S1A and S1B)

Is contour of the nasal tip symmetric? (focus on infratip lobule, ignoring the nostrils)

- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs

YES



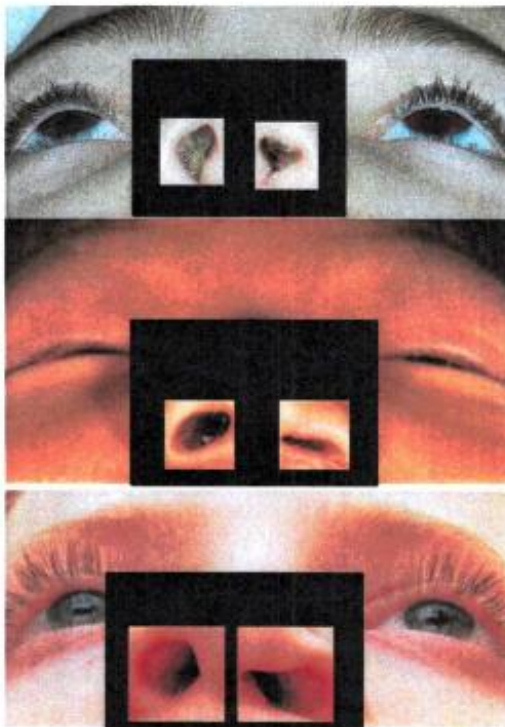
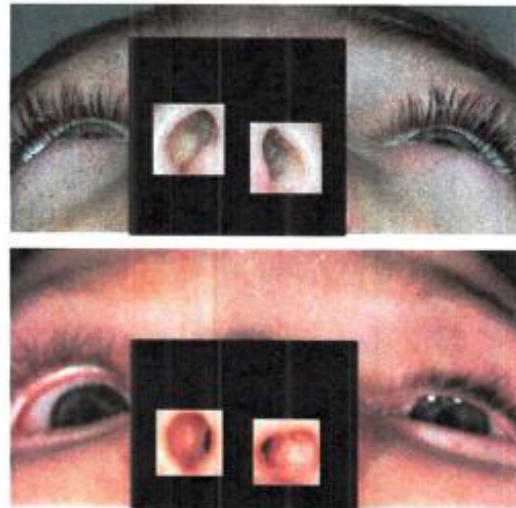
NO



Q2: Nostril Circumference (use Folders S1A and S1B)

Is there a substantial micro-nostril or macro-nostril? (consider nostril size and ignore nostril shape)

- ☐ YES
- ☐ NO
- ☐ Can not evaluate, because _____

Reference PhotographsYESNO

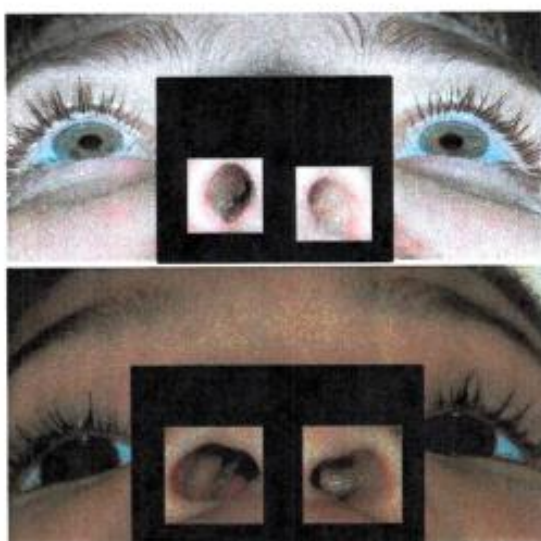
Q3: Nostril Rim Shape Symmetry (use Folders S1A and S1B)

Do the nostril rims have similar shapes? (evaluate shape of the entire nostril rim)

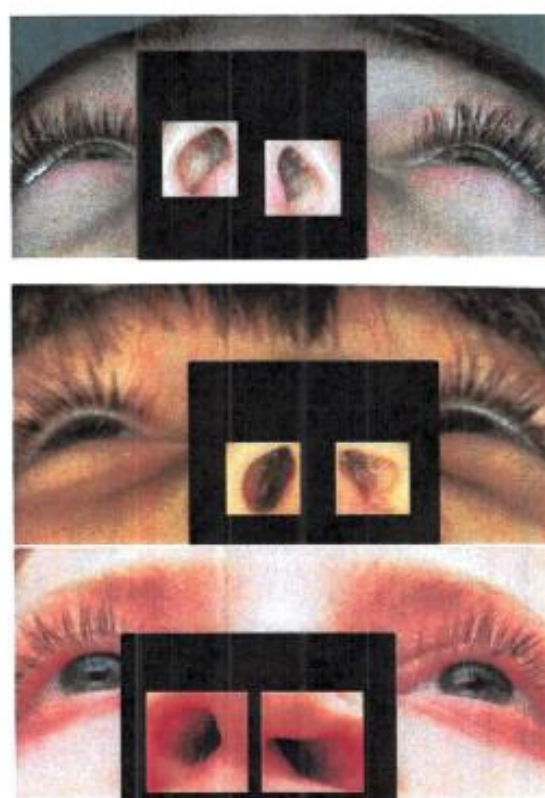
- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs

YES



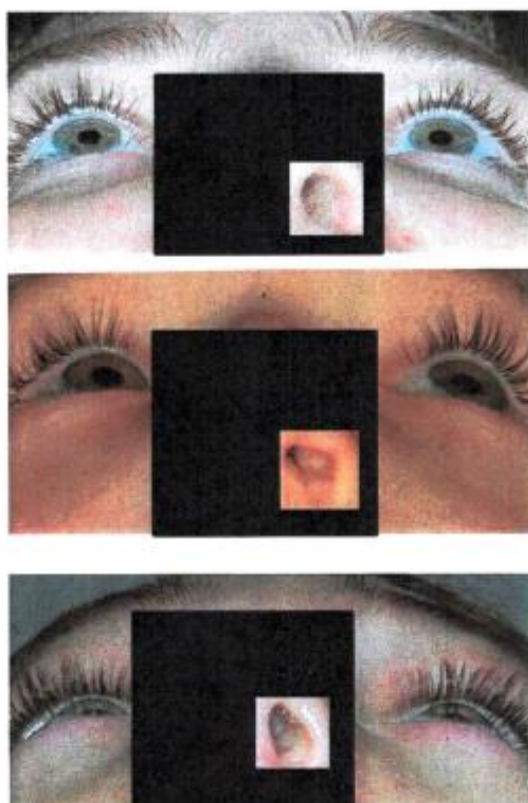
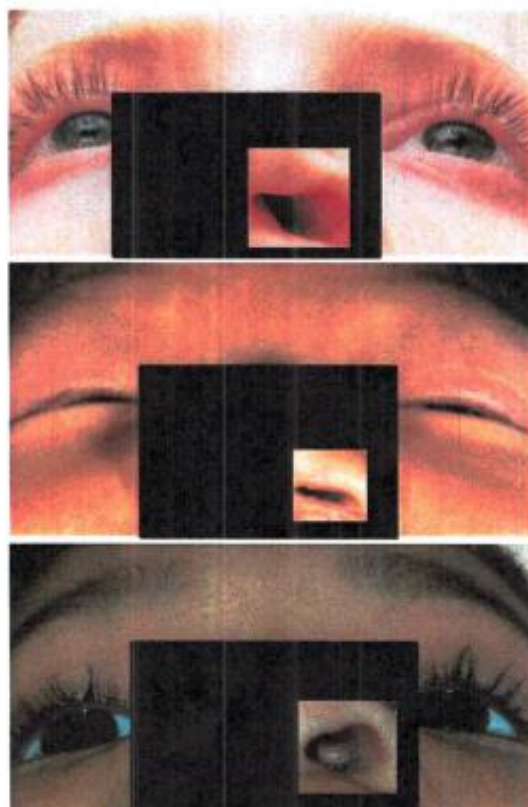
NO



Q4: Recurvatum of cleft-side nostril (use Folders S2A and S2B)

Looking at the anterior portion of the nostril rim, does the rim have a smooth concave shape?

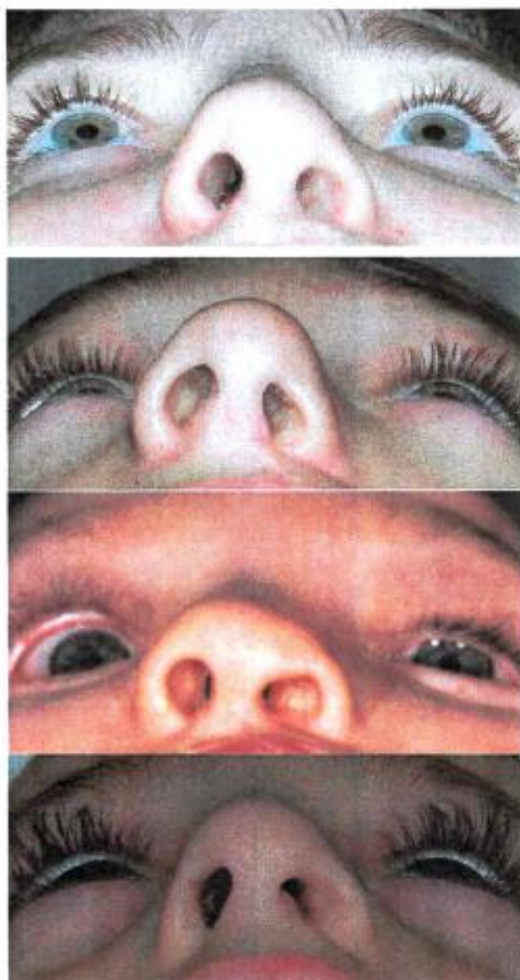
- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs**YES****NO**

Q5: Columnella Angulation (use Folders S2A and S2B)

Is the columnella perpendicular to a line connecting the lateral canthi? (ignore the nasal footplate; if the columnella appears twisted more than 15 degrees then consider the columnella angulated and respond NO)

- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference PhotographsYESNO

Q6: **Balanced Cupid's Bow** (use Folders F1A and F1B)

Are the peaks of Cupid's bow at the same vertical level, within 0.5 mm? (The peak of cupid's bow is the most cephalad point of the vermillion-cutaneous junction.)

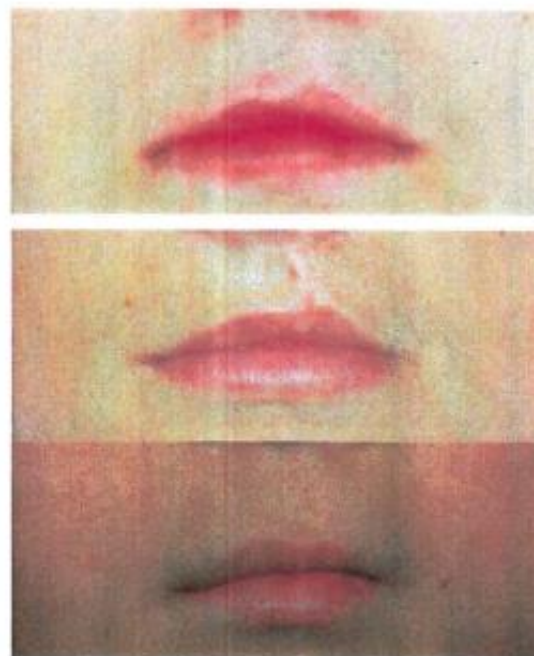
- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs

YES



NO



Q7: **Vermillo-Cutaneous Junction** (use Folders F1A and F1B)

Is there a stair-step present in the vermillo-cutaneous junction of the upper lip?

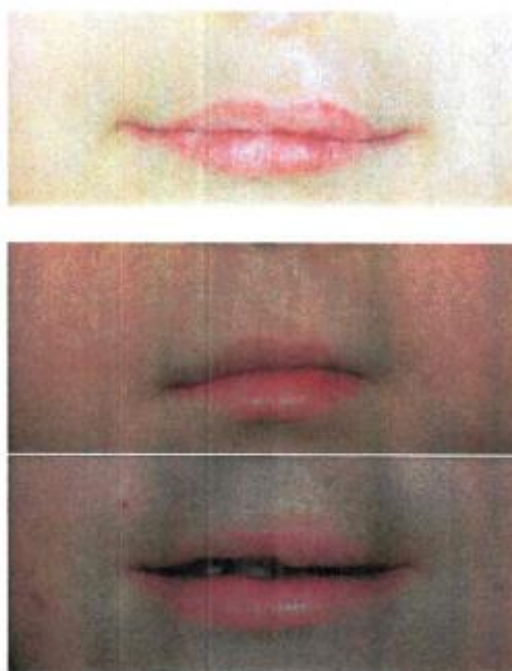
- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs

YES



NO



Q8: Vermillo-Mucosal Junction – Stairstep (use Folders F1A and F1B)

Is there a stair-step present in the vermillo-mucosal junction of the upper lip? (if the picture does not show the vermillo-mucosal junction, response "can not evaluate")

- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference Photographs**YES****NO**

Q9: Alar Base Overall Symmetry (use Folders F2A and F2B)

Are the alar bases symmetric in their position and how they insert into the cheek?

- ☐ YES
☐ NO
☐ Can not evaluate, because _____

Reference PhotographsYESNO

Q10: Scar Position – Location (use Folders F2A and F2B)

Does the majority of the scar lie along natural lines?

☐ YES

☐ NO

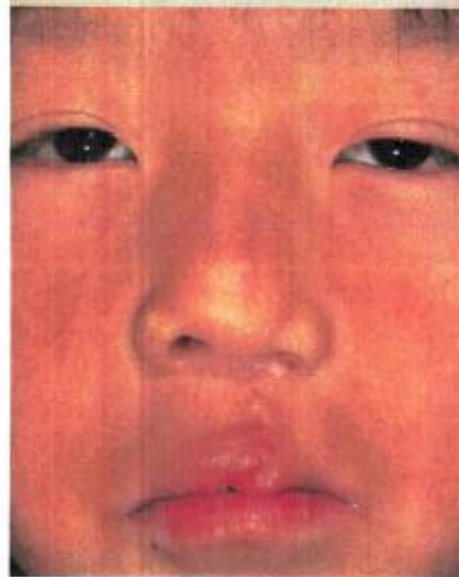
☐ Can not evaluate, because _____

Reference Photographs

YES



NO



Q11: **Scar Quality Overall** (use Folders F2A and F2B)

Overall is this a good or favorable scar?

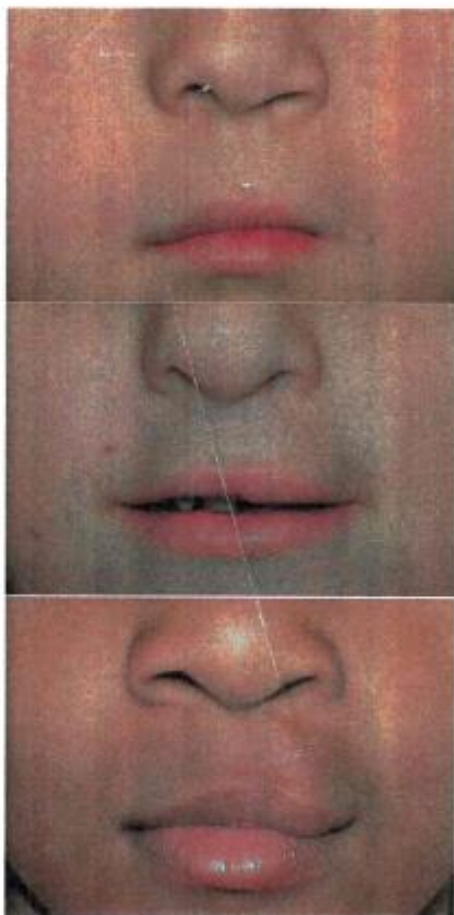
☐ YES

☐ NO

☐ Can not evaluate, because _____

Reference Photographs

YES



NO



Ethics Approval



Date: 3 May 2019

To: Dr. Damir Matic

Project ID: 113883

Study Title: Longterm Outcomes of Using Presurgical Infant Orthopaedic Devices in Cleft Palate

Application Type: HSREB Initial Application

Review Type: Delegated

Meeting Date / Full Board Reporting Date: 21/May/2019

Date Approval Issued: 03/May/2019

REB Approval Expiry Date: 03/May/2020

Dear Dr. Damir Matic

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Latham vs NAM Data Collection Form V1	Other Data Collection Instruments	16/Apr/2019	1
Latham vs NAM Protocol V1	Protocol	16/Apr/2019	1

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
References	References	11/Apr/2019	1

No deviations from, or changes to, the protocol or WREM application should be initiated without prior written approval of an appropriate amendment from Western HSREB, except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Daniel Wyzynski, Research Ethics Coordinator, on behalf of Dr. Joseph Gilbert, HSREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

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1.10 Figure 1



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1.11 Figure 11

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Curriculum Vitae: Katie Garland

EDUCATION

PGY3 Plastic and Reconstructive Surgery <i>University of Western Ontario, London, ON</i>	2018- 2023
Masters of Surgery <i>University of Western Ontario, London, ON</i>	2019- 2020
Doctor of Medicine <i>University of Ottawa, Ottawa, ON</i>	2014- 2018
Bachelor of Science, Physiology (Honors) <i>McGill University, Montreal, QC</i>	2010- 2014

ACADEMIC HIGHLIGHTS & AWARDS

Bootcamp for Resident Teachers Bootcamp for residents nominated for their interest in teaching <i>Schulich School of Medicine and Dentistry, London, ON</i>	2019
Global Health International Elective Bursary (\$1000) Awarded to select students for participation in global medical electives <i>Faculty of Medicine, University of Ottawa, ON</i>	2018
Dean's Honor List Top 10% of graduating students in the Faculty of Science <i>Faculty of Science, McGill University, QC</i>	2010- 2014
McGill Physiology Honors Program Selected based on academic excellence (10 of 150 students selected) <i>Faculty of Science, McGill University, QC</i>	2012- 2014
Respiratory Epidemiology and Clinical Research Unit Research Award (\$3000) Awarded in support of student research project (2 awards given) <i>Respiratory Epidemiology and Clinical Research Unit, McGill University, QC</i>	2013

RESEARCH PUBLICATIONS

1. **Garland K**, Chen BP, Roffey DM, Poitras S, et al. "How accurate is administrative coding in detecting adverse events after elective orthopaedic surgery?" *Canadian Journal of Surgery*. 2020; 63(1): E35-37.
2. **Garland K**, Matic D. "Current Approaches to cleft lip revision." *Current Opinion Otolaryngology Head and Neck Surgery*. 2019; 27(4):287-293.
3. Gawad N, Head L, McGuire C, Gangemi A, **Garland K**, et al. "Branches From the "SEAD": Sustained and Feasible Expansion of the Surgical Exploration and Discovery (SEAD) Program." *Journal of Surgical Research*. 2018; 235:315-321.
4. **Garland K**, Nahiddi N, Trull B, Malic C. "Pediatric Burns: Clinico-epidemiological Evaluation via an Outpatient Database." *Burns Journal*. 2018; 204-207.
5. Andrioli V, Guerra L, Keays M, Keefe D, Tang K, Sullivan K, **Garland K**, et al. "Active surveillance for antenatally detected ureteroceles: Predictors of success." *Journal of Pediatric Urology*. 2018; 14(3) : 243.e1-243.e6.
6. Chen BP, **Garland K**, Roffey DM, Poitras S, Dervin G, Lapner P, et al. "Can Surgeons Adequately Capture Adverse Events Using the Spinal Adverse Events Severity System (SAVES) and OrthoSAVES?" *Clinical orthopaedics and related research*. 2017;475(1):253-60.
7. Labonte LE, Bourbeau J, Daskalopoulou SS, Zhang M, Coulombe P, **Garland K**, et al. "Club Cell-16 and RelB as Novel Determinants of Arterial Stiffness in Exacerbating COPD Patients." *PloS one*. 2016;11(2):e0149974.

SELECT RESEARCH ABSTRACTS AND PRESENTATIONS

1. **Garland K**, Matic D. "Comparing dental occlusion outcomes in cleft lip and palate patients with different presurgical orthopedic devices."
 - Oral presentation: Canadian Society of Plastic Surgeons; Jun. 2020; online due to Covid-19
2. Chambers S, **Garland K**, Delyzer T. "Adherence of clinical referrals to ABA criteria in a tertiary care burn centre: A retrospective review."
 - Poster presentation: Canadian Society of Plastic Surgeons; Jun. 2020; online due to Covid-19
 - Awarded runner-up for best poster in resident competition
3. **Garland K**, Matic D. "Anatomic and surgical predictors of velopharyngeal insufficiency following primary cleft palate repair."
 - Accepted for oral presentation (canceled due to Covid-19): American Cleft Palate Association; Apr. 3rd, 2020; Portland, OR

4. **Garland K**, Truong J, Matic D. "Safety and outcomes of Latham appliance in a consecutive series of unilateral cleft lip in a single surgeon's practice."
 - Oral presentation: Canadian Society of Plastic Surgeons; Jun. 28th, 2019; St. John's, NL
5. **Garland K**, Chen B, Roffey DM, Poitras S, Wai E, Kingwell S, Beaulé PB. "How Accurate is Administrative Coding in Detecting Adverse Events After Elective Orthopaedic Surgery?"
 - Oral presentation: American Association of Orthopaedic Surgery; Mar. 6th, 2018; New Orleans, LA, USA
6. Malic C, **Garland K**, Nahiddi N, Trull B. "Pediatric Burns: Clinico-epidemiological evaluation via an outpatient database"
 - Oral presentation: Canadian Burn Symposium; Sept. 25th, 2017; Toronto, ON
7. **Garland K**, Trull B, Nahiddi N, Malic C. "Pediatric hand burns: does dressing choice impact outcomes?"
 - Poster presentation: American Society for Surgery of the Hand; Sept. 8th, 2017; San Francisco, CA, USA
8. **Garland K**, Trull B, Nahiddi N, Malic C. "Pediatric burns: does dressing choice impact outcomes?"
 - Poster presentation: The 8th World Congress on Paediatric Burns; June 22nd, 2017; Birmingham, UK
9. **Garland K**, Roffey D, Phan P, Wai E, Kingwell S. "Comparison of adverse event recording tools during a ten-week prospective pilot study in elective spine surgery patients at a tertiary spine centre."
 - Oral presentation: Canadian Orthopaedic Association; June 17th, 2016; Quebec City, QC
10. Chen B, **Garland K**, Roffey D, Poitras S, Lapner P, Dervin G, Phan P, Wai E, Kingwell S, Beaulé P. "A Pilot Study of the Usability and Viability of Adverse Event Recording Tools in Elective Spine and Orthopaedic Surgery Patients."
 - Oral presentation: Canadian Orthopaedic Association; June 21st, 2017; Quebec City, Quebec